Stereoselective Synthesis of Chiral Tetra(Tertiary Phosphines)

By Swarup Chatterjee

A Thesis
Submitted for the Degree of
Doctor of Philosophy
of
The Australian National University

January 2001

The work described herein is the author's own work, unless otherwise stated, and was carried out within the Department of Chemistry, The Faculties, Australian National University. None of this material has been submitted in support of a submission for any other degree.

S Chatterjee

ACKNOWLEDGEMENTS

I would like to take this opportunity to firstly give my sincere thanks to Geoff Salem. His supervision, guidance and friendship over the course of my studies has been very much appreciated. I would also like to thank Roy Doyle for all his help and advice and interesting discussions throughout this research project.

I would like to express my gratitude and give thanks to Tony Willis, of the Research School of Chemistry, for the time and effort he put into solving the crystal structures shown in this thesis. Thanks also to Paul Gugger, of the RSC, for providing valuable pieces of equipment and amounts of resolving agent, and Tin Culnane for running variable temperature NMRs for me.

I would like to give thanks to my friends and colleagues throughout the Department of Chemistry. In particular, thanks to my fellow group members over the years; Mark George, Felicity Moore, Natalie Ward, Justine Bennett and Leah Walker, and to my fellow PhD students Jason Chaplin, Michael Ernst-Russell, Paul Huleatt, Damien Kuzek, Simone Louwhoff and Nigel Lucas, for their friendship, support, long lunches and conversations which made the last three and a half years so enjoyable. My thanks also to the academic and technical staff in the Department, for all their assistance and encouragement over the years, and for making the Department such a great place to work.

I would finally like to thank my parents and my brother Taposh for all they have done for me. I could never have got this far without them.

ABSTRACT

The secondary phosphine (±)-(2-dimethylphosphinophenyl)methylphosphine has been prepared by reaction of the bis(secondary phosphine) (R_P*,R_P*)- and (R_P*,S_P*)-1,2-phenylenebis(methylphosphine) with 1.2 equivalents of potassium in liquid ammonia, followed by the addition of methyl iodide. The product typically contained *ca* 20-25% of the di(tertiary phosphine) 1,2-phenylenebis(dimethylphosphine). Subsequent reaction of the secondary phosphine with sodium in THF, followed by addition of 1,2-dichlorobenzene, gave the asymmetric di(tertiary phosphine) (±)-(2-chlorophenyl)(2-dimethylphosphinophenyl)-methylphosphine in 65% yield. The resolution of the racemic di(tertiary phosphine) has been achieved *via* the separation, by fractional crystallisation, of a 1:1:1:1 mixture of four diastereomeric palladium(II) salts containing the ligand and optically active ortho-metalated (*S*)-N,N-dimethyl[1-(1-naphthyl)ethyl]amine. The absolute configuration of the R_P enantiomer of the di(tertiary phosphine) was determined by X-ray analysis of the least soluble diastereomeric palladium(II) complex, [SP-4-3]-(S_P,*S*)-[(2-chlorophenyl)(2-dimethylphosphinophenyl)methylphosphine-P,P']{[(1-dimethylamino)-ethyl]naphthyl-C^2,N}palladium(II) hexafluorophosphate.

Two chiral tetra(tertiary phosphines) (R_P*,R_P*)-1,2-bis[(2-dimethylphosphinophenyl)methylphosphino]benzene [(R_P*,R_P*)-**57**] and (R_P*,R_P*)-1,2-bis[(2-diphenylphosphinophenyl)methylphosphino]benzene [(R_P*,R_P*)-**58**] have been synthesised in a completely stereoselective manner. The related ligand (R_P*,R_P*,R_P*,S_P*)-1,2-bis-[(2-methylphenylphosphino)methylphosphino]benzene [(R_P*,R_P*,R_P*,S_P*)-**59**], the first example of a linear tetra(tertiary phosphine) with four phosphorus stereocentres, was synthesised with high stereoselectivity, a *ca* 9:1 mixture of (R_P*,R_P*,R_P*,S_P*)-**59** and (R_P*,S_P*,S_P*,R_P*)-**59** being formed. The tetra(tertiary phosphine) (R_P*,R_P*)-**57** was synthesised by the coupling of (±)-(2-chlorophenyl)(2-dimethylphosphinophenyl)methylphosphine with sodium (2-dimethylphosphinophenyl)methylphosphide [generated *in situ* by deprotonation of (±)-(2-dimethylphosphinophenyl)methylphosphine with sodium], in THF at -78 °C. The tetra(tertiary phosphine) was separated from 1,2-

phenylenebis(dimethylphosphine), which was present as an impurity, by complexation to cobalt(III). The related chiral tetra(tertiary phosphines) (R_P*,R_P*)-**58** and **59** were synthesised by an alternative route, by reaction of sodium 1,2-phenylenebis(methylphosphide) [generated *in situ* by reaction of the bis(secondary phosphine) (R_P*,R_P*)- and (R_P*,S_P*)- 1,2-phenylenebis(methylphosphine) with two equivalents of sodium in THF] with two equivalents of (2-chlorophenyl)diphenylphosphine or (±)-(2-chlorophenyl)methylphenylphosphine, respectively, in THF. The ligand (R_P*,R_P*)-**58** was isolated as a microcrystalline white solid, in 33% yield. The two diastereomeric forms of **59** have been isolated by complexation to cobalt(III) and the diastereomeric cobalt(III) complexes were separated by column chromatography.

All of the tetra(tertiary phosphines) adopted the *cis*-α configuration exclusively upon coordination to cobalt(III), as confirmed by the X-ray crystal structure determinations of *cis*-α-[$CoCl_2${(R_P*,R_P*)-**57**)}]PF_6, *cis*-α-[$CoCl_2${(R_P*,R_P*)-**58**}]Cl and *cis*-α-[$CoCl_2${(R_P*,R_P*,R_P*,S_P*)-**59**}]PF_6. The presence of three 1,2-phenylene linkages in the ligand backbone is believed to be responsible for the high stereoselectivity observed in the synthesis of the quadridentate ligands and in the exclusive formation of the cis-α diastereomer upon co-ordination to cobalt(III). Chiral tetra(tertiary phosphines) that are generated stereoselectively and which form the *cis*-α diastereomer in octahedral metal complexes are potential chiral auxiliaries in asymmetric synthesis.

The co-ordination of (R_P*,R_P*)-**58** to gold(I), silver(I) platinum(II) and ruthenium(II) has also been investigated. Monomeric tetrahedral complexes were prepared by reaction of (R_P*,R_P*)-**58** with tetrabutylammonium diiodoaurate in ethanol, or silver nitrate in ethanol, followed by metathesis with ammonium hexafluorophosphate. The structure of the gold(I) complex [Au{(R_P*,R_P*)-**58**}]PF_6 has been determined by X-ray crystallography and is the first mononuclear gold(I)-tetra(tertiary phosphine) complex to have been structurally authenticated. A mixture of two silver(I) complexes have been isolated, and the structure of one of the silver(I) complexes has been determined by X-ray crystallography, revealing a mononuclear complex containing (R_P*,R_P*)-**58** in which insertion of two oxygen atoms has occurred

between the metal and the internal phosphorus atoms of the ligand. The other silver(I) complex is believed to be [Ag{(R_P*,R_P*)-**58**}]PF_6. A mononuclear platinum(II) complex *cis*-[$PtMe_2${(R_P*,R_P*)-**58**}], where the tetra(tertiary phosphine) is co-ordinated to the metal centre through the internal phosphorus atoms only, was formed from the reaction of [$PtMe_2$(COD)] with (R_P*,R_P*)-**58** in *n*-pentane. The ruthenium(II) complex *cis*-α-[$RuCl_2${(R_P*,R_P*)-**58**}] was prepared by reaction of $RuCl_2(DMSO)_4$ with (R_P*,R_P*)-**58** in methanol, followed by addition of concentrated hydrochloric acid.

These complexes indicate the propensity of tetradentate ligands of this type to form mononuclear complexes with transition metal ions. This can be attributed to the rigidity of the ligand imposed by the 1,2-phenylene rings in the ligand backbone. This is in contrast with other tetra(tertiary phosphines) which have more flexible alkyl groups in the ligand backbone and often form binuclear complexes.

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STEREOCHEMICAL NOMENCLATURE

The stereochemical nomenclature used in this work is consistent with that used in the most recent *Chemical Abstracts Index Guide*.[, 1999 #189] The following is a summary of relevant guidelines for the application of stereochemical descriptors.

(i) Assignment of absolute configuration by the descriptors R and S conforms to the sequence rule specifications Cahn, Ingold and Prelog (CIP).

(ii) The relative descriptors *R** and *S** are similar to R and S but are relative in the sense that the lowest number (first cited, highest priority) asymmetric centre is arbitrarily assigned an *R** descriptor. For example, a compound assigned the relative descriptor (*R*,R**) contains two stereocentres having the same absolute configuration, either both *R* or both *S*. In a similar fashion, the relative descriptor (*R*,S**) implies that one stereocentre is *R* and the other *S*. An identical argument applies for compounds with three or more stereocentres.

(iii) These descriptors are used to relate the total stereochemical information for a compound as follows:

a) When only one chiral element is present in the molecule, the absolute descriptor is cited as (*R*)- or (*S*)- . If two or more chiral elements are present, the reference centre which is of highest rank according to the sequence rule (CIP) is assigned an R or S descriptor.

b) Optical rotation [descriptors (±)-, (-)- and (+)-]; When the absolute stereochemistry is described as in a) the sign of rotation can be omitted. For molecules having more than one chiral element the sign of rotation is cited together with a relative descriptor.

(iv) The absolute descriptor is cited first, followed by the relative descriptor, if any, in parentheses. The entire descriptor set is then enclosed in brackets. For

example, a molecule containing two chiral centres of the same helicity, say R, the stereochemical descriptors preceding the name or the formula of the substance and the optical information will be given as thus: [*R*-(*R**,*R**)]-(+)- or [*R*(*R**,*R**)]-(-)-.

(v) For coordination compounds, however, additional descriptors are necessary to completely describe the stereochemistry. For mononuclear complexes there is a system indicator to express the molecular geometry of the molecule. For example, for two-coordinate linear molecules the descriptor used is L-2 while for four coordinate tetrahedral molecules the descriptor is T-4.

LIST OF ABBREVIATIONS

aq	aqueous
Bu	butyl
Bz	benzyl
COD	1,5-(cyclooctadiene)
diars	1,2-phenylenebis(dimethylarsine)
e.e.	enantiomeric excess
EI-MS	Electron Impact Mass Spectrometry
Et	ethyl
EtOH	ethanol
GABOB	4-amino-3-hydroxybutyric acid
GC-MS	Gas Chromatography-Mass Spectrometry
h	hours
Me	methyl
MeOH	methanol
MeI	methyl iodide

m/e	Mass/charge
mins	minutes
mmp	mitochondrial membrane potential
n-Bu	n-butyl
NMR	Nuclear Magnetic Resonance
i-Pr	isopropyl
Ph	phenyl
THF	tetrahydrofuran
TMEDA	tetramethylethylenediamine

Chapter One

Introduction

1.1 HISTORICAL INTRODUCTION

1.1.1 Synthesis and Co-ordination Chemistry of Tertiary Phosphines

There is a rich and extensive chemistry associated with the synthesis and co-ordination chemistry of tertiary phosphines. In their optically pure form, such compounds are not only of intrinsic interest in inorganic chemistry, but have been very effective as chiral auxiliaries in asymmetric synthesis and catalysis.

The history of tertiary phosphines dates back to 1847, beginning with the synthesis of trimethylphosphine by Paul Thérnard, who passed chloroform over calcium phosphide at 180-300 °C.[2] Significant advances in the synthesis of alkyl-substituted tertiary phosphines were achieved by Hofmann and Cahours[3] in the latter part of the 19th century, while Michaelis concurrently developed routes to aryl-substituted tertiary phosphines, including the preparation of triphenylphosphine in 1885.[4] The impetus for much of this research was to investigate the relationship between the chemistry of amines and their phosphine counterparts. However, these early examples of tertiary phosphines often proved hazardous to synthesise and difficult to purify and characterise, and while their ability to combine with heavy metal salts was noticed almost immediately, this aspect of their chemistry was initially not widely studied.

The development of organo-arsenic and -sulfur chemistry, prompted by the discovery of their cytotoxic properties and their use as chemical warfare agents during World War I, led to rapid advances in organophosphorus chemistry in the early 20th century. The concurrent growth in these areas of chemistry, and the observation that such ligands could solubilise metal ions in organic solvents, lead to improved synthetic methods for a range of monodentate tertiary phosphines and set the scene for the development of their coordination chemistry.[5]

A major difference between tertiary phosphines and amines is that although both have pyramidal geometries, the respective rates of inversion are markedly different. The rate of pyramidal inversion of amines is rapid at room temperature [E_{inv} (amine) *ca* 25 kJ mol^{-1}], whereas for phosphines, the rate is immeasurably slow at room temperature [E_{inv} (phosphine) *ca* 120 kJ mol^{-1}].[6] Consequently, phosphines have a fixed pyramidal structure and are configurationally stable in their enantiomerically pure forms at ambient temperatures. Meisenheimer and Lichtenstadt achieved the first resolution of an organophosphorus compound in 1911 with the resolution of (±)-ethylmethylphenylphosphine oxide.[7] It was not until 1961, however, when Horner discovered that optically active phosphonium salts containing a benzyl group could be electrolytically reduced at a mercury cathode with removal of the benzyl group to give optically active phosphines, that the first optically active tertiary phosphines were obtained.[8] Phosphorus stereochemistry is one of the most important aspects of modern phosphorus chemistry, with optically pure phosphines being utilised as chiral auxiliaries in asymmetric synthesis, and in the elucidation of reaction mechanisms and biological transformations.[6]

Advances in the coordination chemistry of tertiary phosphines have opened up a number of interesting and important avenues of research. Phosphine ligands have been found to stabilise a range of metal complexes containing unstable molecules as co-ligands, such as dinitrogen complexes,[9] metal hydride complexes, metal alkyl and aryl complexes,[10] as well as stabilising unusually high, or low, oxidation states of metals. In recent times, transition metal-phosphine complexes [in particular, gold(I) complexes of di- and tetra-(tertiary phosphines)] have shown great potential as anticancer agents.[11-13] The most important area of research with these compounds, however, has been in homogenous and heterogeneous catalysis, and the use of optically pure transition metal-phosphine complexes in asymmetric synthesis and catalysis.[5] Literally hundreds of optically active bidentate tertiary phosphines have been synthesised and utilised as chiral auxiliaries in asymmetric catalysis. Much of the research to date on the coordination chemistry of tertiary phosphines has focussed on complexes containing monodentate or bidentate tertiary phosphines.

Initial interest in the contemporary transition metal chemistry of tertiary phosphines, and arsines, was developed by Mann in the 1930s.[14,15] Jensen worked extensively on the stereochemistry of metal-phosphine complexes[16] and observed the ability of phosphine ligands to stabilise metals in high oxidation states.[17] After World War II, further significant advances in the coordination chemistry of both phosphines, and arsines, were made by Dwyer,[18] Chatt and Nyholm.[19] The properties of phosphine and arsine ligands, as discovered by these research groups, lead to an explosion of interest in the synthesis and co-ordination chemistry of both monodentate and multidentate phosphines. The excellent ligation properties of phosphines were attributed to the sigma donation of the phosphorus lone pair to an empty orbital on the metal, and the pi back-donation from a filled metal orbital to the antibonding σ^* orbital of the phosphorus atom, to provide a strong metal-ligand bond. By altering the nature of the substituents of the phosphorus atom, phosphine ligands were found to exhibit a range of sigma-donor and pi-acceptor abilities, in effect tuning the electronic properties of the metal centre.

The predictable stereochemical and electronic properties of metal complexes containing phosphine ligands demanded the development of viable synthetic routes to poly(tertiary phosphines). Prior to the 1960s the only general route to such compounds was the reaction between alkali metal phosphides, or Grignard reagents, with haloorganic compounds. Phosphides of the type $M[PPh_2]$ (M = Li, Na, K) were of particular utility as their preparation from commercially available triphenylphosphine was well established. Dramatic advances in ^{31}P and ^{13}C NMR spectroscopy, and X-ray crystallography, aided in the development of new synthetic routes, as well as allowing detailed probing of the structure, bonding and stereochemical aspects of transition metal-phosphine complexes. Newer, more versatile routes were developed throughout the 1960s and 1970s, lead by the research groups of King, Meek, Venanzi and Sacconi. A range of methods now exist for the synthesis of poly(tertiary phosphines), the most important being: (i) the base-catalysed addition of P-H bonds across the C=C moiety in vinyl phosphines; (ii) the AIBN-initiated free radical-catalysed addition of P-H bonds to the C=C moiety of allyl- and vinyl-phosphines; (iii) the phosphonium route to chiral unsymmetrical bidentate phosphines; (iv) high-dilution synthesis; the reaction of phosphorus

nucleophiles with halogenated or tosylated hydrocarbons to give macrocyclic poly(tertiary phosphines); and (v) the template synthesis of poly(tertiary phosphines), in particular, macrocycles.[20-22]

The synthesis of chiral poly(tertiary phosphines) *via* currently available synthetic routes involves the separation of two or more diastereomeric forms of the ligand prior to resolution of the racemic entities. The most common method of resolution involves the conversion of the racemic compound to a pair of diastereomers, by reaction with an enantiopure auxiliary. The chiral auxiliary can be covalently bonded to, co-ordinated to, or form a salt with, the racemic compound. The diastereomers are then separated by one of a number of methods, including fractional crystallisation, distillation, extraction and various forms of chromatography.[23] The most successful method of resolution of tertiary phosphines involves fractional crystallisation of a pair of diastereomers derived from the racemic phosphine and an optically active transition metal complex. Whilst a number of unidentate and bidentate tertiary phosphines have been resolved in this manner, there are relatively few examples of optically active poly(tertiary phosphines). The primary aim of the research work described herein is the development of a stereoselective route towards the synthesis of chiral tetra(tertiary phosphines).

1.2 TERTIARY PHOSPHINES IN ASYMMETRIC SYNTHESIS

1.2.1. Historical Background

The initial work with phosphine ligands in catalysis began in the 1940's, with Reppe's discovery that such ligands enhanced the activity of some nickel based polymerisation and carbonylation catalysts.[5] In the 1950's, after Ziegler's discovery that the reaction of triethylaluminium with certain zirconium or titanium compounds gave polyethylene,[24] Natta used triphenylphosphine to solubilise the metal ion in solution, under reducing conditions, and extended the versatility of the process to make

polypropylene and other polymers.[25] The major breakthrough in homogenous catalysis, however, was made in 1968, beginning with the work of Wilkinson and co-workers, who reported that chlorotris(triphenylphosphine)rhodium(I) catalysed the hydrogenation of alkenes at low temperatures.[26]

Horner *et al.* further reported that analogues of Wilkinson's catalyst containing the optically active tertiary phosphine (*R*)-methylphenyl-*n*-propylphosphine catalysed the hydrogenation of 2-phenylbutene in an enantioselective manner.[27] Knowles *et al.* reported that the same complex catalysed the hydrogenation of 2-phenylacrylic acid enantioselectively.[28] The enantiomeric excesses were low in both cases, but compared well to similar work using Grignard reagents derived from optically active alkyl halides and encouraged further research into the area of asymmetric catalysis using transition metal-phosphine complexes.

In 1972, Knowles used a rhodium(I) complex containing (*R*)-(1,2-anisyl)cyclohexylmethylphosphine [(*R*)-CAMP] to catalyse the hydrogenation of various acylphenylalanine precursors, with optical yields that approached 90%.[29] Rhodium(I) catalysts containing optically active monodentate tertiary phosphines, however, typically gave low enantioselectivities. The low asymmetric inductions were attributed to conformational lability with the degree of asymmetric induction being reduced as the number of diastereotopic interactions between substrate and complex increased. The subsequent use of more structurally rigid rhodium(I)-diphosphine complexes reduced the number of diastereomeric interactions and gave uniformly higher enantiomeric excesses, in some cases greater than 95%.[30,31]

1.2.2 Di(tertiary phosphines) in Asymmetric Catalysis

Optically active di(tertiary phosphines) have proven to be the most successful chiral auxiliaries used in asymmetric catalysis to date. In particular, asymmetric hydrogenation has been the most intensely studied and most successful process. The standard for the evaluation of new catalyst systems is the asymmetric hydrogenation

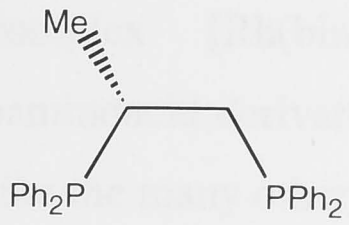
of N-acyldehydro-α-amino acids. Enantioselective excesses approaching 100% have been achieved with certain rhodium(I)-diphosphine systems.[32,33]

The great strength of utilising di(tertiary phosphines) as chiral auxilaries is the ability to tailor ligands of this type so as to enhance the reactivity and selectivity of the catalysts. Only slight changes in the ligand structure can cause great changes in selectivity.[34] Over 1000 chiral diphosphine ligands have been synthesised and utilised as chiral auxiliaries in asymmetric catalysis, with varying degrees of effectiveness. Some of the most successful di(tertiary phosphines) utilised as chiral auxiliaries in asymmetric catalysis are shown in Figure 1.

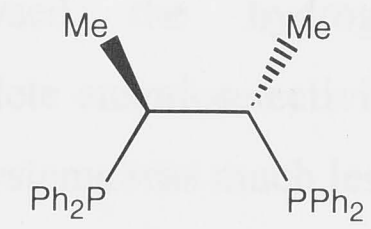
The vast majority of these ligands have non-stereogenic phosphorus donor atoms and the donor group is typically the diphenylphosphino moiety. The chirality invariably stems from the presence of carbon stereocentres in the backbone of the ligands. The di(tertiary phosphines) (R_P,R_P)-dipamp [(R_P,R_P)-**6**] and (*S*)-binap [(*S*)-**5**] do not contain any carbon stereocentres. Dipamp has stereogenic phosphorus donor atoms, and binap is chiral due to the restricted rotation about the bond between the naphthyl groups.

1.2.3 Binap: the Most Successful Chiral Auxiliary in Asymmetric Catalysis

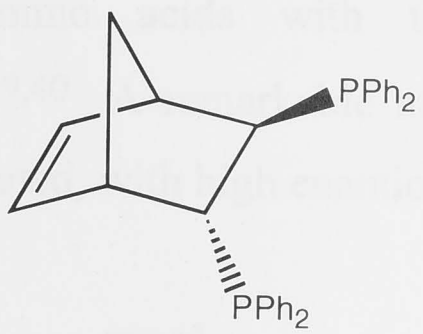
Of the ligands **1-8**, binap (**5**), developed by Noyori and co-workers, has proven to be the most successful of the di(tertiary phosphines) to be used as chiral auxiliaries in asymmetric catalysis to date. A number of reviews have appeared in the literature on the role of binap as a chiral auxiliary in asymmetric synthesis.[35-37]



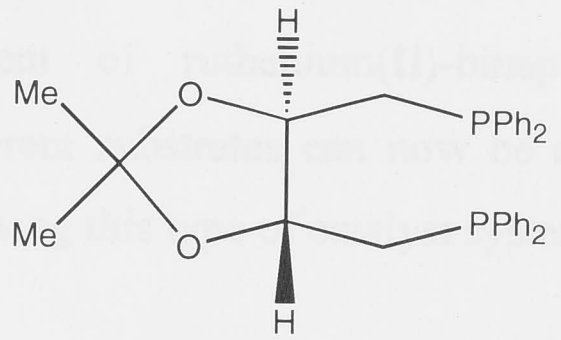
(*R*)-Prophos [(*R*)-**1**]



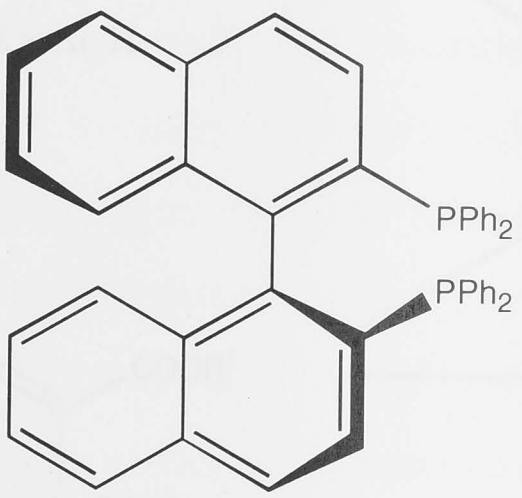
(*S,S*)-Chiraphos [(*S,S*)-**2**]



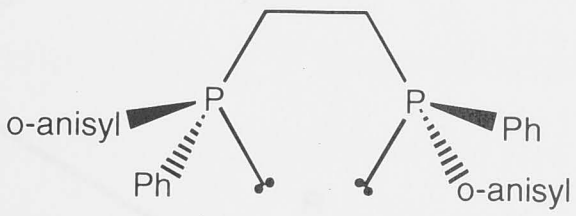
(*R,R*)-Norphos [(*R,R*)-**3**]



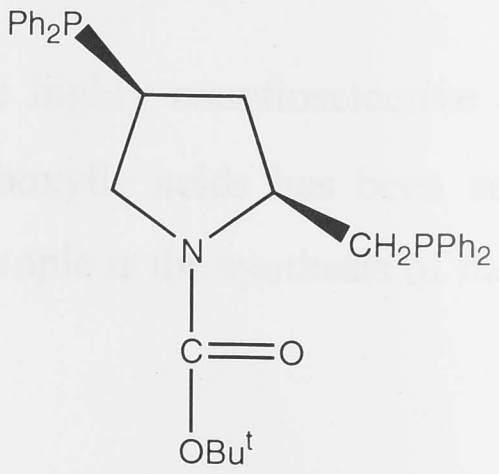
(*R,R*)-Diop [(*R,R*)-**4**]



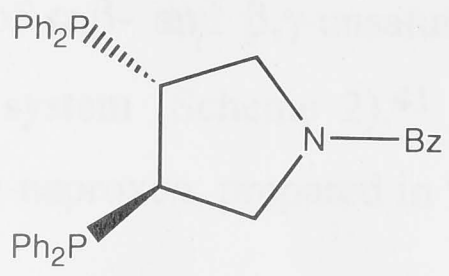
(*S*)-Binap [(*S*)-**5**]



(R_P,R_P)-Dipamp [(R_P)-**6**]



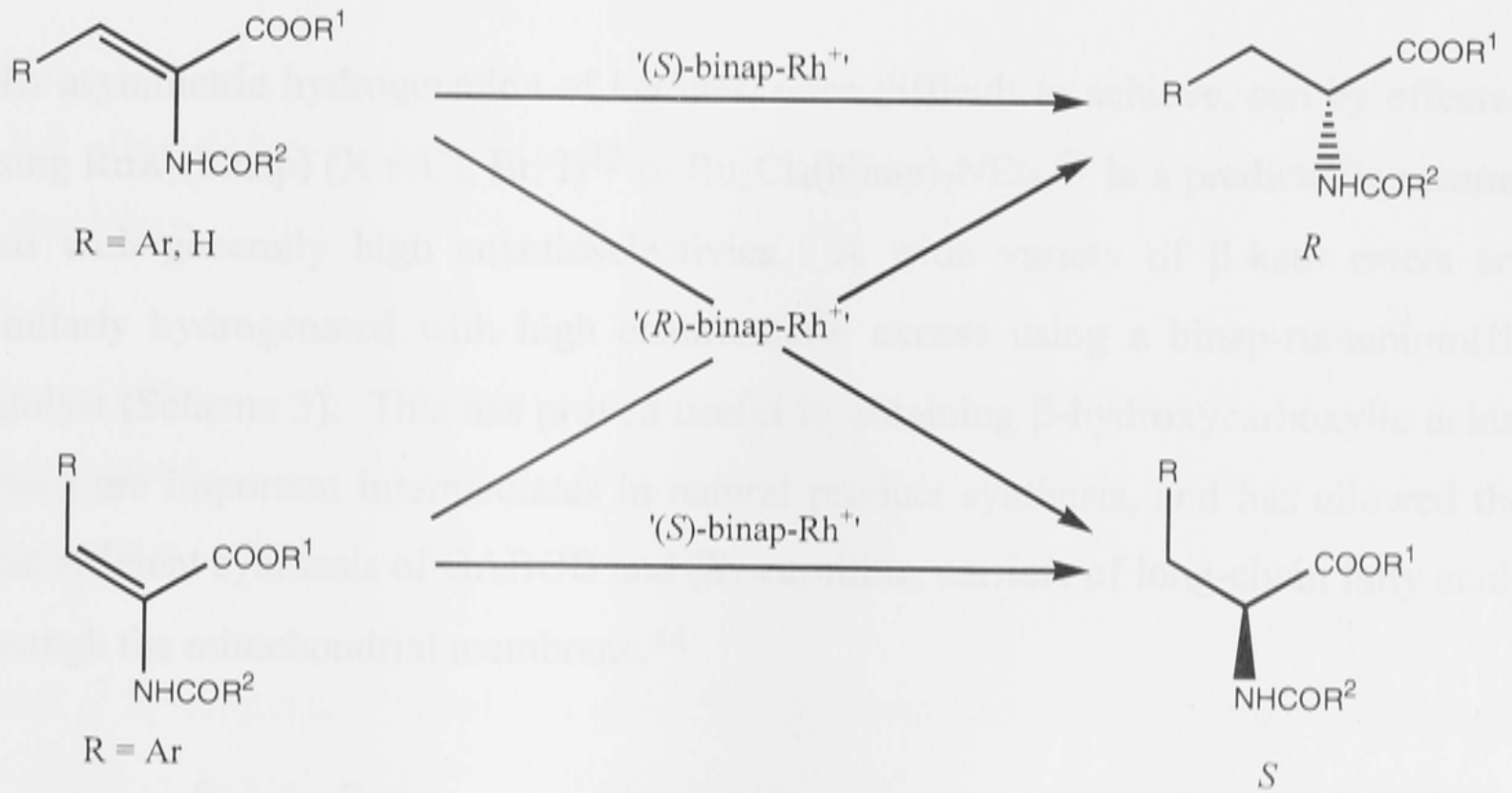
(*S,S*)-BPPM [(*S,S*)-**7**]



(*R,R*)-Pyrphos [(*R,R*)-**8**]

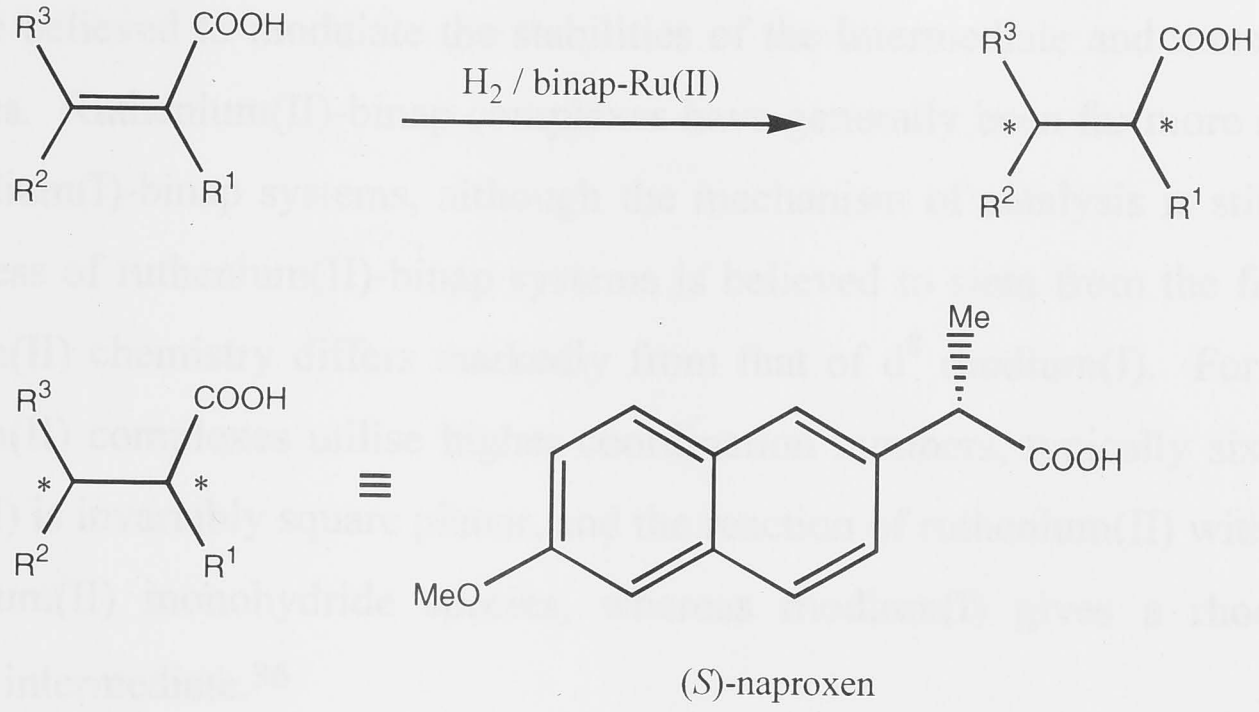
Figure 1 Some examples of optically active di(tertiary phosphines) that have been successful as chiral auxiliaries in asymmetric catalysis.

The complex $[Rh(binap)(MeOH)_2]ClO_4$ catalysed the hydrogenation of dehydroaminoacid derivatives with essentially complete enantioselectivities (Scheme 1), but like the many other rhodium(I)-diphosphine systems was much less impressive in the catalytic hydrogenation of a range of other substrates. For example, the same system catalyses the hydrogenation of geraniol or nerol with only 70% e.e.[38] The utility of binap in asymmetric hydrogenation, however, has been extended far beyond dehydroamino acids with the development of ruthenium(II)-binap catalyst systems.[39,40] A remarkable number of different substrates can now be efficiently hydrogenated, with high enantioselectivities, using this type of catalyst system.



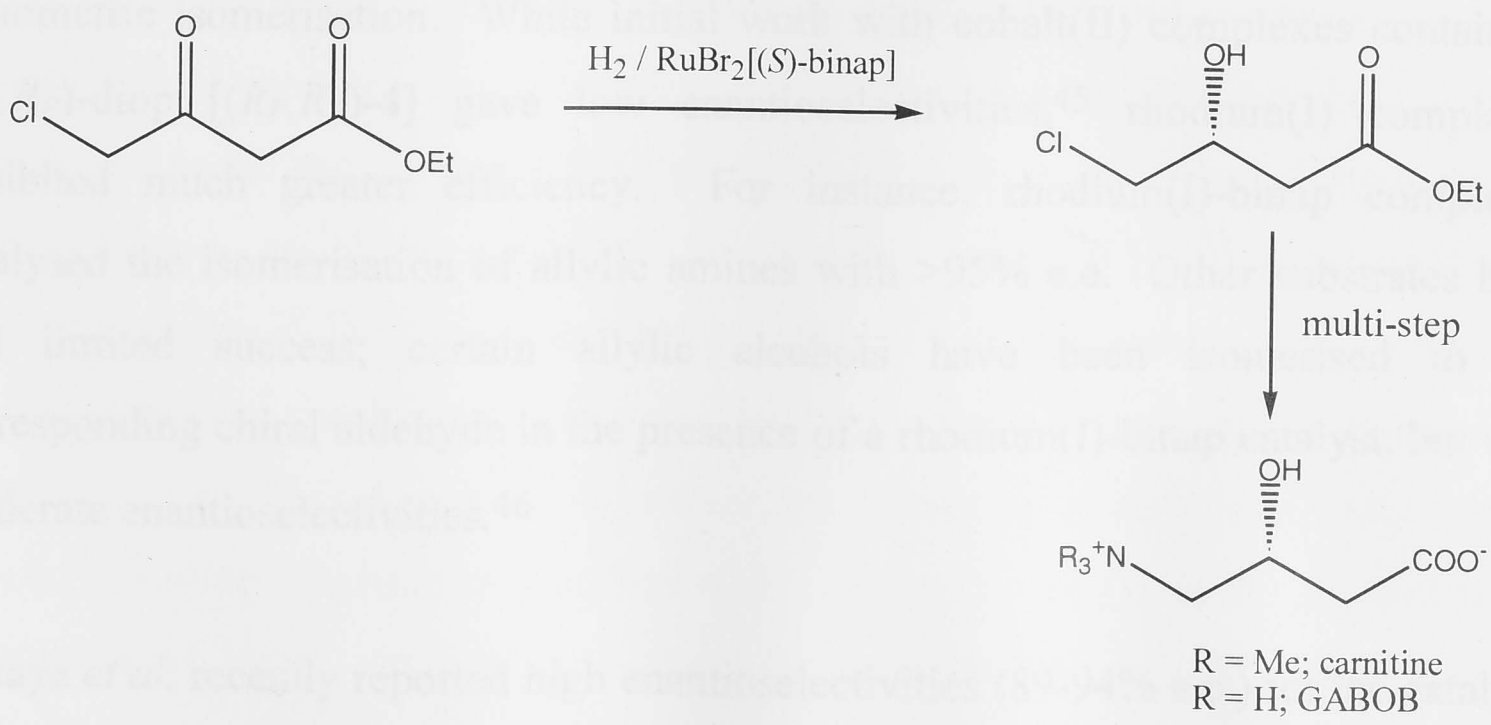
Scheme 1

The highly enantioselective hydrogenation of a range of α,β- and β,γ-unsaturated carboxylic acids has been achieved using this catalyst system (Scheme 2).[41] An example is the synthesis of the anti-inflammatory drug (*S*)-naproxen, prepared in 97% e.e.



Scheme 2

The asymmetric hydrogenation of ketones, once difficult to achieve, can by effected using RuX_2(binap) (X = Cl, Br, I)[42] or $Ru_2Cl_4(binap)_2NEt_3$,[43] in a predictable manner and with generally high enantioselectivies. A wide variety of β-keto esters are similarly hydrogenated with high enantiomeric excess using a binap-ruthenium(II) catalyst (Scheme 3). This has proved useful in obtaining β-hydroxycarboxylic acids, which are important intermediates in natural product synthesis, and has allowed the first efficient synthesis of GABOB and (*R*)-carnitine, carriers of long-chain fatty acids through the mitochondrial membrane.[44]



Scheme 3

The success of binap as a chiral auxiliary may be attributable to the degeneracy caused by its C_2 symmetry, which minimises the number of diastereomeric reactive intermediates and transition states. The phenyl rings attached to the phosphorus

atoms are believed to modulate the stabilities of the intermediate and transition state complexes. Ruthenium(II)-binap complexes have generally been far more successful than rhodium(I)-binap systems, although the mechanism of catalysis is still unclear. The success of ruthenium(II)-binap systems is believed to stem from the fact that d^6 ruthenium(II) chemistry differs markedly from that of d^8 rhodium(I). For example, ruthenium(II) complexes utilise higher coordination numbers, typically six, whereas rhodium(I) is invariably square planar, and the reaction of ruthenium(II) with H_2 gives a ruthenium(II) monohydride species, whereas rhodium(I) gives a rhodium(III)-dihydride intermediate.[36]

1.2.4 Other Asymmetric Reactions Catalysed by Transition Metal-Phosphine Complexes

Many transition metal-phosphine complexes have been studied as catalysts in a range of asymmetric reactions with varying degrees of success. Some notable examples are discussed below.

The 1,3 hydrogen shift of allylic amines is the most successful example of catalytic asymmetric isomerisation. While initial work with cobalt(II) complexes containing (R_P,R_P)-diop [(R_P,R_P)-**4**] gave low enantioselectivities,[45] rhodium(I) complexes exhibited much greater efficiency. For instance, rhodium(I)-binap complexes catalysed the isomerisation of allylic amines with >95% e.e. Other substrates have had limited success; certain allylic alcohols have been isomerised to the corresponding chiral aldehyde in the presence of a rhodium(I)-binap catalyst, but with moderate enantioselectivities.[46]

Takaya *et al.* recently reported high enantioselectivities (89-94% e.e.) for the catalytic asymmetric hydroformylation of styrene and its derivatives using a rhodium(I) complex containing the chiral phosphine-phosphite ligand (*R,S*)-binaphos [(*R,S*)-**9**], shown in Figure 2.[47] Stille had previously reported the hydroformylation of vinyl acetate using a Pt/Sn catalyst with (*S,S*)-BPPM [(*S,S*)-**7**], in 96% e.e.[48,49]

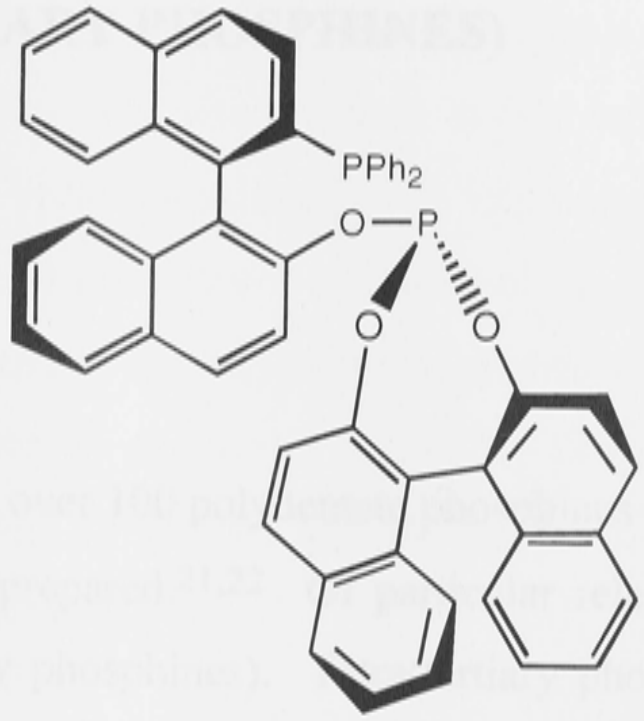


Figure 2 The chiral phosphine-phosphite ligand (*R,S*)-Binaphos [(*R,S*)-**9**].

Other asymmetric transformations catalysed by transition metal-phosphine complexes include catalytic asymmetric hydrosilylation, where palladium complexes of binaphthyl-containing monodentate tertiary phosphines have been used to catalyse the hydrosilation of 1-alkenes and norbornadiene with 96% e.e.[50,51] Certain ruthenium(II)-(*R*)-binap complexes have also been used in the kinetic resolution of racemic alcohols, where under appropriate conditions, the enantiomers of racemic allylic secondary alcohols react at sufficiently different rates with the chiral auxiliary to provide a means of resolution.[52]

While di(tertiary phosphines) have been well studied and utilised in asymmetric catalysis, there are very few examples of ligands of higher denticity having been investigated in the same regard. Several tripodal ligands with C_3 symmetry have had limited success as chiral auxiliaries in catalytic asymmetric hydrogenation and hydroformylation.[20,53] Cotton and Hong (1992)[21] have comprehensively reviewed the synthesis, structural aspects, and selected applications of polydentate phosphines with three to six phosphorus donor atoms. In contrast to monodentate, and to some extent, bidentate phosphines, analogues of higher denticity offer a number of advantages as chiral auxiliaries or stereochemical probes, including an increased nucleophilicity at the metal centre, greater control of the coordination number, stoichiometry and stereochemistry of the resulting metal complexes, slower and more controlled intra- and inter-molecular exchange reactions, and useful detailed structural and bonding information from phosphorus-phosphorus coupling constants in NMR spectra.[21]

1.3 TETRA(TERTIARY PHOSPHINES)

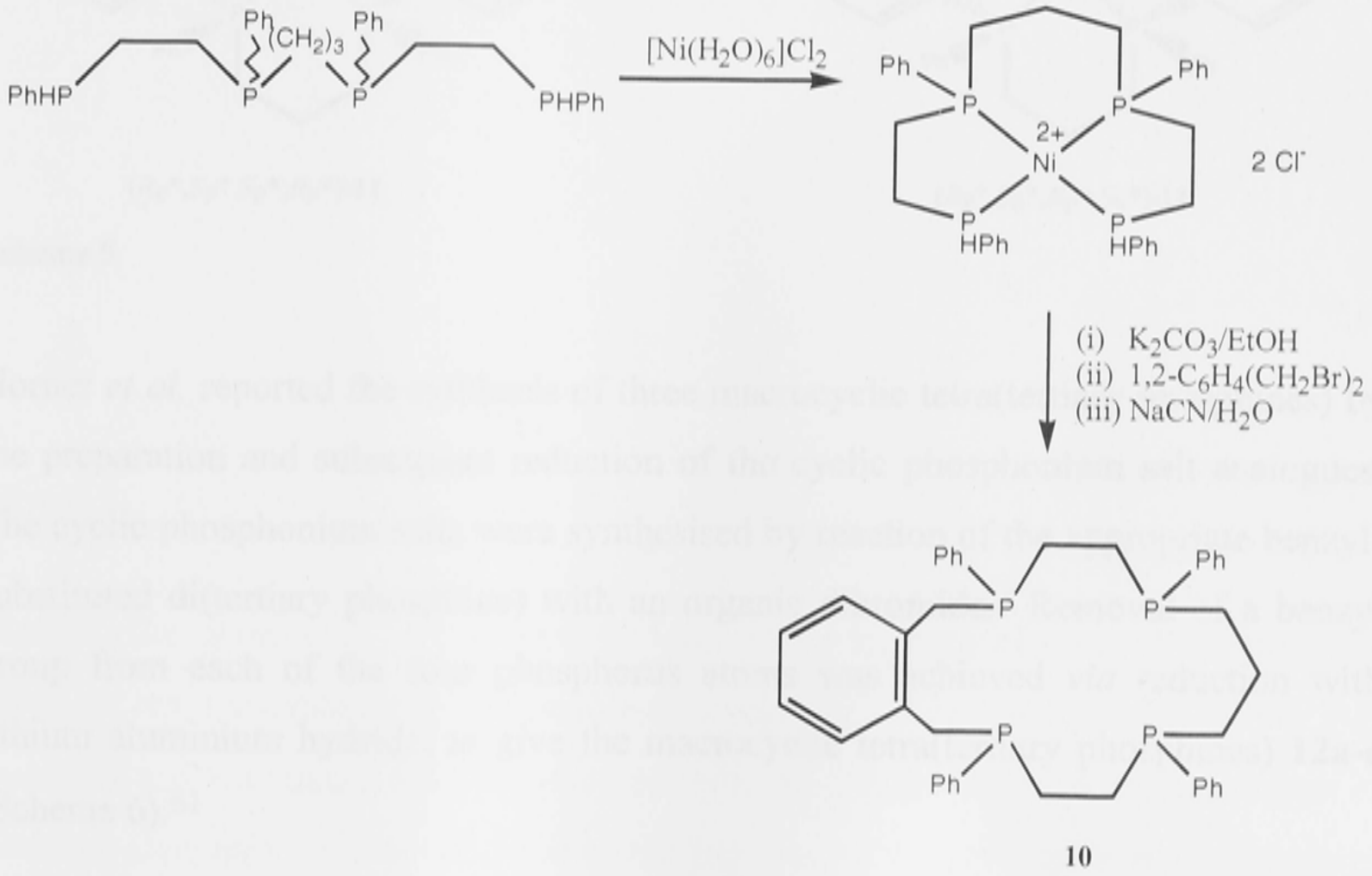
1.3.1 General

In the past three decades, over 100 polydentate phosphines containing 3-6 phosphorus donor atoms have been prepared.[21,22] Of particular relevance to this work is the chemistry of tetra(tertiary phosphines). Tetra(tertiary phosphines) can be classified into (i) macrocyclic tetra(tertiary phosphines); (ii) tripodal tetra(tertiary phosphines); (iii) spirocyclic and branched tetra(tertiary phosphines); and (iv) facultative (linear) tetra(tertiary phosphines).

1.3.2 Macrocyclic Tetra(Tertiary Phosphines)

The chemistry of macrocycles with phosphorus donor atoms, including tetra(tertiary phosphine) macrocycles, has not been developed to the same extent as analogous ligands containing nitrogen, oxygen or sulfur donor atoms, primarily due to the poor yields obtained for both the ligands and their complexes and the requirement of multi-step syntheses involving difficult-to-handle phosphine precursors.[22] However, phosphorus-containing macrocycles are of intrinsic interest due the profound steric and electronic influence of such ligands when coordinated to metal ions. Furthermore, Kyba *et al.* have shown that while 11-membered macrocycles with P3 donor sets are too small to encapsulate transition metal ions, 14 membered macrocyles with P4 donor sets are the optimum ring size for metal binding.[54] The synthesis of phosphorus-containing macrocyles and cryptands, including tetra(tertiary phosphines) of this type, has recently been reviewed.[55] The synthetic methods available for the formation of such ligands are either conventional (classical) macrocyclic synthesis, reduction of cyclic phosphonium salts, or metal-template based methods.

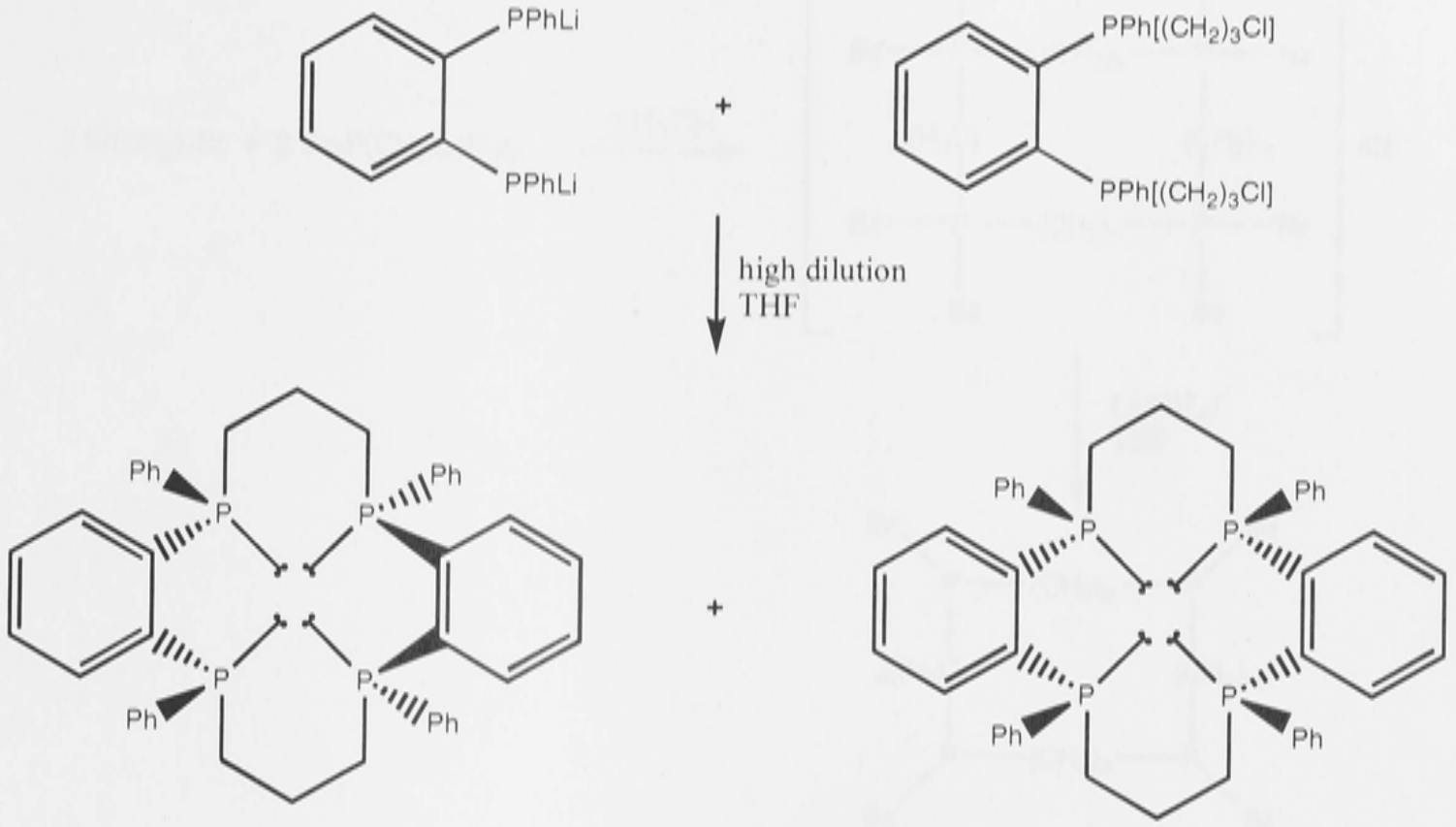
Although the first phosphorus-containing macrocycles were prepared in 1897,[56] it was not until the 1970s that intensive research in this area began, when Horner and co-workers incorporated phosphorus atoms into macrocycles in 1975,[57] and Berlin and coworkers described the synthesis of a number of P_4 phosphonium macrocycles in 1976.[58] The first macrocyclic tetra(tertiary phosphines) were reported, however, by the research groups of Rosen and Kyba in 1977. The macrocylic ligand **10** was prepared by DelDonno and Rosen *via* a metal template synthesis on nickel(II) to achieve ring closure (Scheme 4).[59]



10

Scheme 4

Kyba also reported the synthesis of the 14-membered P_4 macrocycle **11**. The final cyclisation step of the multi-step synthesis was the reaction of lithium 1,2-phenylenebis(phenylphosphide) with (R_P*,R_P*)- and (R_P*,S_P*)-1,2-phenylenebis[(3-chloropropyl)phenylphosphine] under high dilution conditions (Scheme 5).[60] Five diastereomers [(R_P*,R_P*,R_P*,R_P*), (R_P*,R_P*,R_P*,S_P*), (R_P*,R_P*,S_P*,S_P*), (R_P*,S_P*,R_P*,S_P*) and (R_P*,S_P*,S_P*,R_P*)] are possible, depending on the disposition of the phenyl groups, but the reaction proved stereoselective with only (R_P*,S_P*,S_P*,R_P*)- and (R_P*,S_P*,R_P*,S_P*)-**11** being formed. The diastereomers were separated by fractional crystallisation from diethyl ether and their structures were determined by X-ray crystallography.[54]

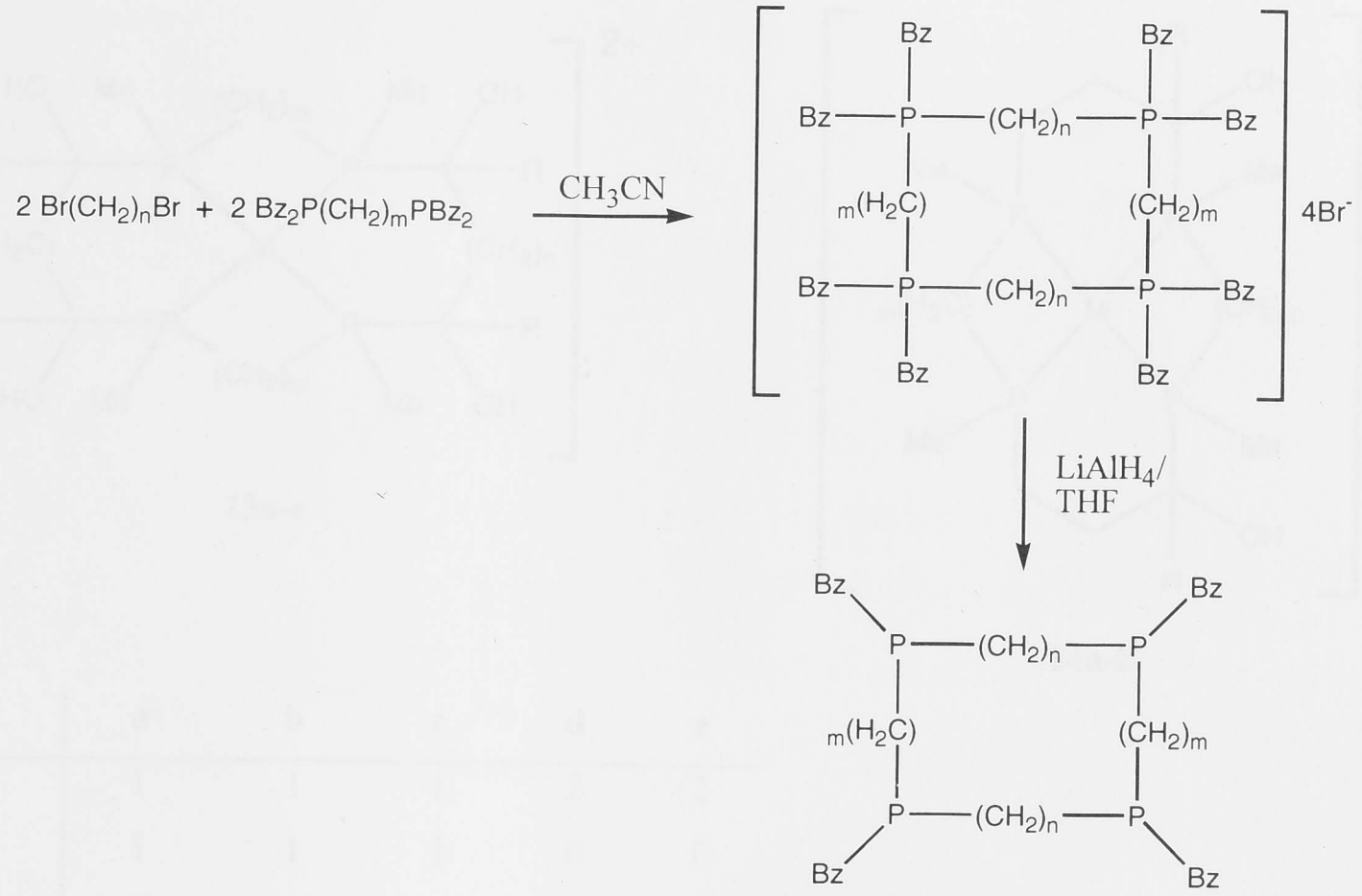


(R_P*,S_P*,S_P*,R_P*)-**11** (R_P*,S_P*,R_P*,S_P*)-**11**

Scheme 5

Horner *et al.* reported the synthesis of three macrocyclic tetra(tertiary phosphines) by the preparation and subsequent reduction of the cyclic phosphonium salt analogues. The cyclic phosphonium salts were synthesised by reaction of the appropriate benzyl-substituted di(tertiary phosphine) with an organic dibromide. Removal of a benzyl group from each of the four phosphorus atoms was achieved *via* reduction with lithium aluminium hydride, to give the macrocyclic tetra(tertiary phosphines) **12a-c** (Scheme 6).[61]

Stelzer *et al.* have reported high yielding routes to a number of P_4 macrocyclic complexes with ethylene and propylene backbones, using a metal-template methodology analogous to that used for macrocyclic amines and imines. The process typically involved formation of bis(bidentate)palladium(II) and nickel(II) complexes containing the bis(secondary phosphines) $MeHP(CH_2)_mPMeH$ (m = 1, 2 or 3), followed by ring closure with the appropriate dialdehydes or diketones $RC(O)(CH_2)_nC(O)R$ (n = 0, 1 and R = H, Me or Ph), to give macrocyclic complexes of the type **13**.[62]

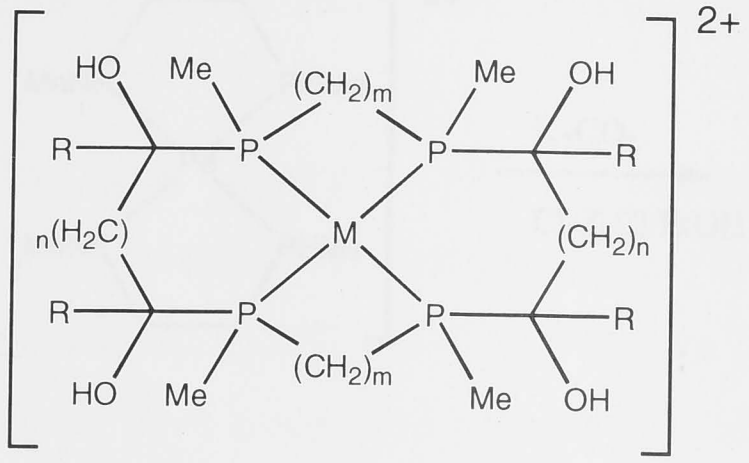


12a-c

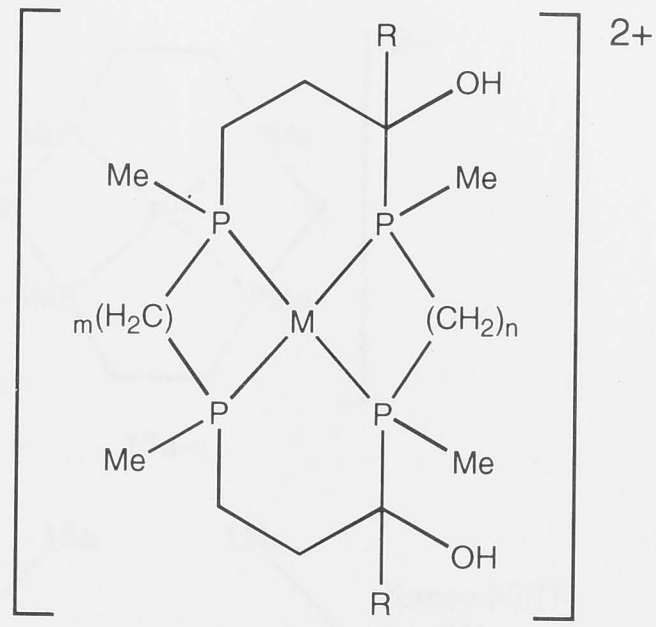
12	a	b	c
m	3	4	3
n	3	4	4

Scheme 6

Macrocyclic complexes of the type **14** were made by ring closure of intermediate acetal or ketyl complexes *via* intramolecular addition of carbonyl groups to the P-H bonds of a co-ordinated bis(secondary phosphine) (Figure 3).[63] A large number of diastereomers may be expected, due to the presence of four phosphorus stereocentres and four stereogenic carbon atoms. The reaction, however, is diastereoselective with only two or three diastereomers formed in each case, although unambiguous identification of these diastereomers has not been reported. Attempts to decomplex the ligands using potassium cyanide proved unsuccessful due to the strong ligand field strength of the co-ordinated macrocycles.



13a-e



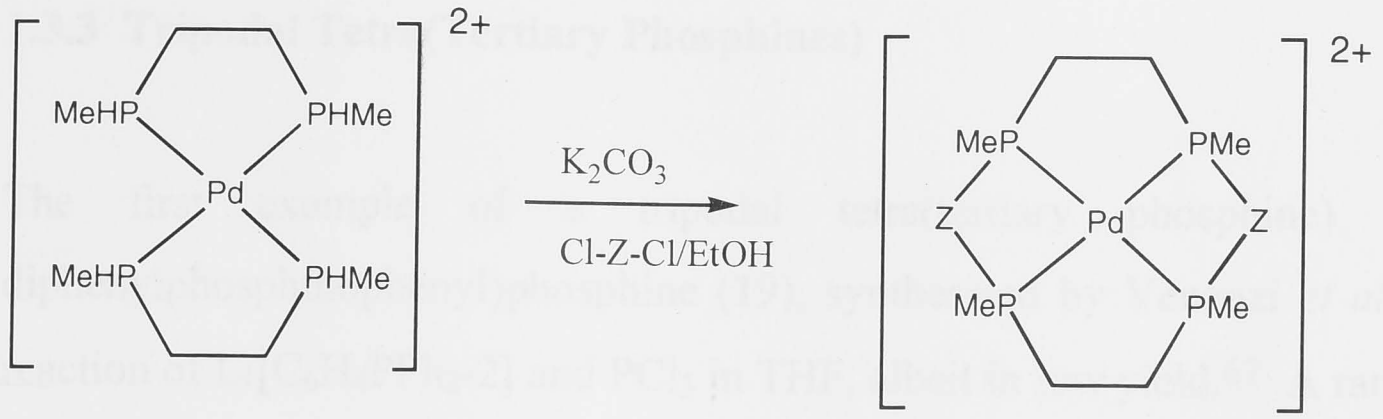
14a-k

13	**a**	**b**	**c**	**d**	**e**
m	1	1	1	2	2
n	1	1	1	0	0
R	H	Me	Me	Me	Ph
M	Pd	Ni	Pd	Pd	Pd

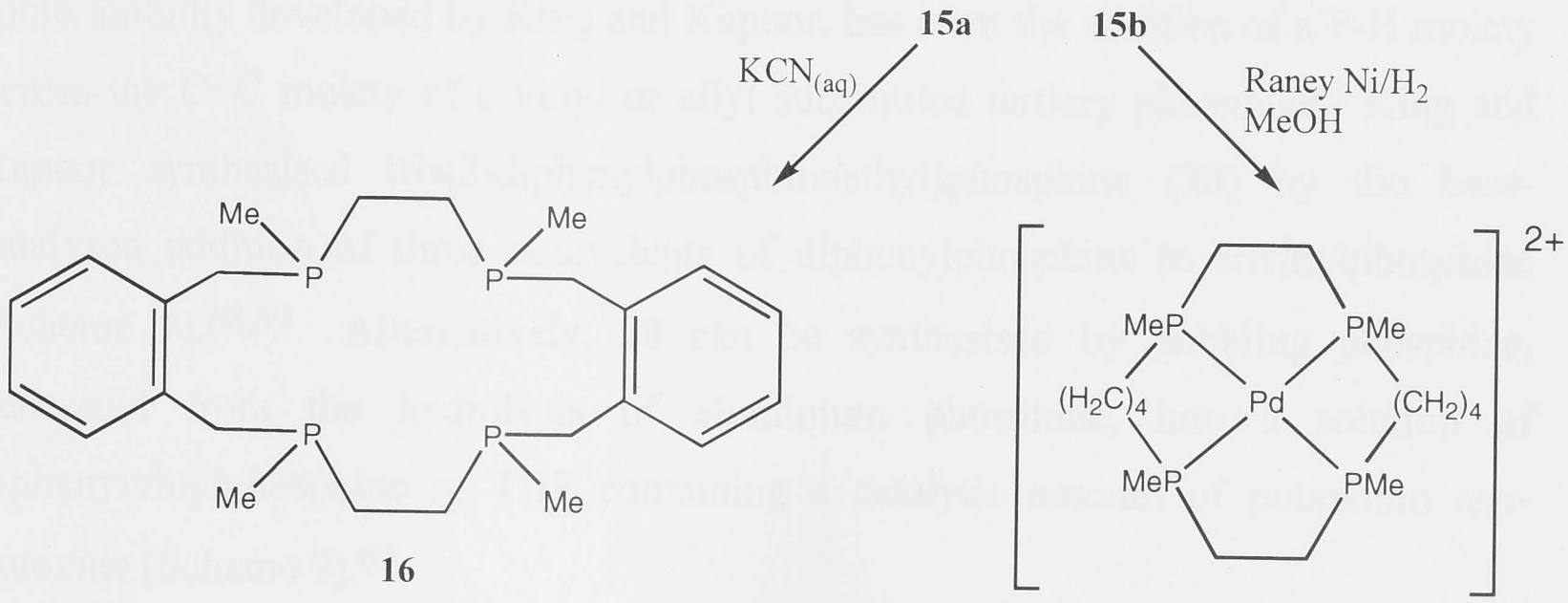
14	**a**	**b**	**c**	**d**	**e**	**f**	**g**	**h**	**i**	**j**	**k**
R	H	H	H	H	Me	Me	Me	Me	Me	Me	Me
M	Ni	Ni	Pd	Pd	Ni	Pd	Pd	Pt	Pt	Pd	Pd
X	Cl	Cl	Cl	Cl	Br	Cl	Cl	Cl	Cl	Cl	Cl
m	2	2	2	2	2	2	2	2	2	3	3
n	2	3	2	3	3	2	3	2	3	2	3

Figure 3 Macrocyclic complexes of the type **13** and **14**.

Another example of metal-template synthesis involves the cyclocondensation of bis(bidentate)palladium(II) complexes of 1,2-bis(methylphosphino)ethane with organic dichlorides to give the macrocyclic complexes **15a-c** (Scheme 7). In the case of **15a** the macrocycle could be decomplexed by treatment with aqueous potassium cyanide to give **16**. The saturated macrocyclic complex **17** was prepared by hydrogenation of **15b** in the presence of Raney nickel.[64,65]

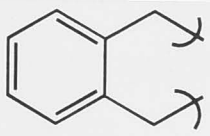
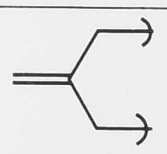


15a-c



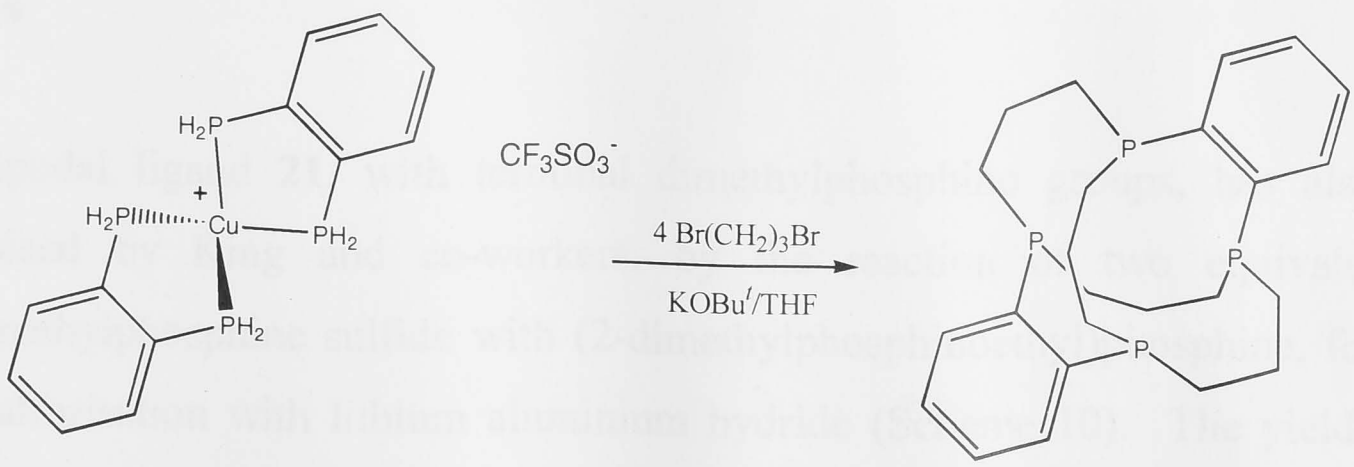
16

17

15	a	b	c
Z			

Scheme 7

The only example of a tetra(tertiary phosphine) cage compound is **18**, prepared by a metal template synthesis [on copper(I)], involving the formation of propylene bridges between two co-ordinated 1,2-phenylenebis(phosphine) ligands using four equivalents of 1,3-dibromopropane (Scheme 8).[66]

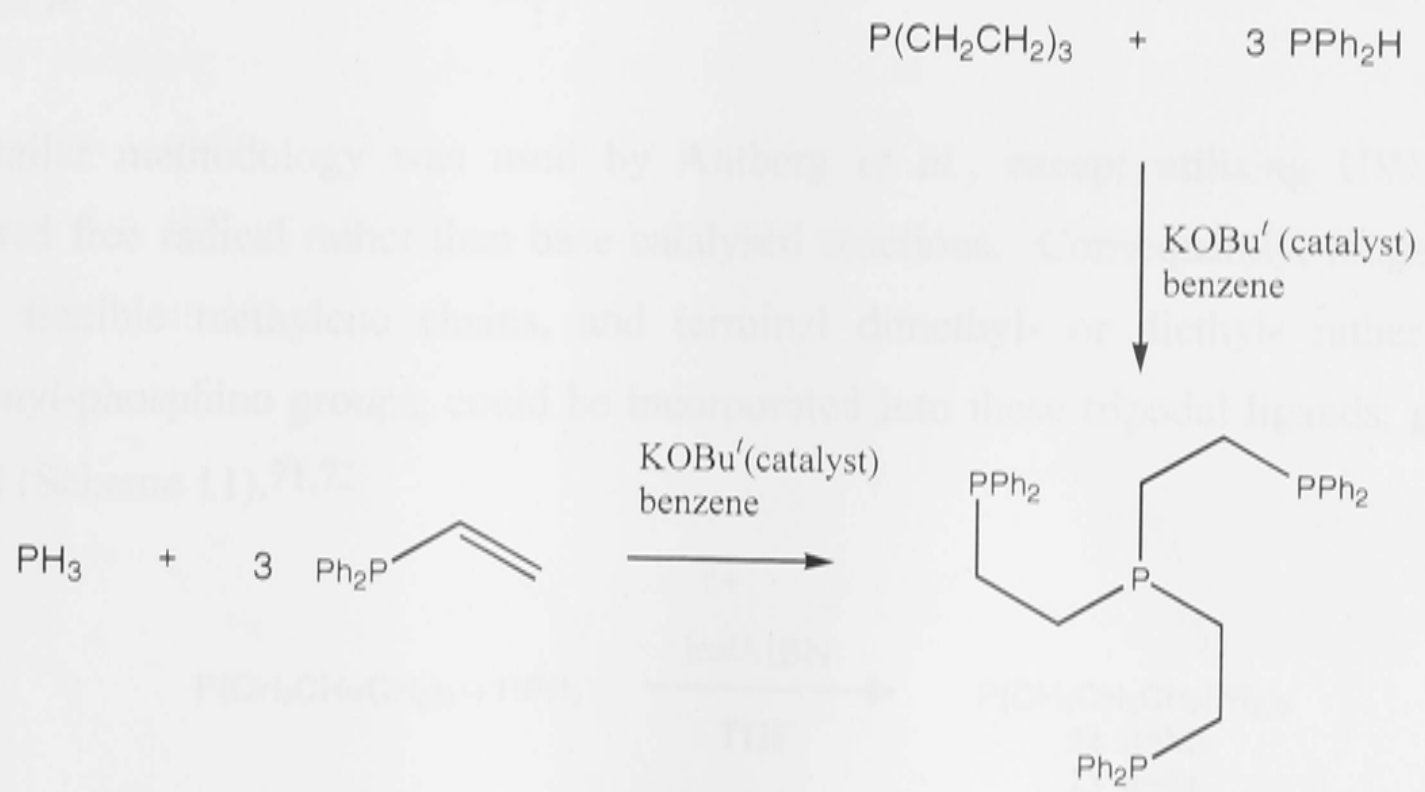


18

Scheme 8

1.3.3 Tripodal Tetra(Tertiary Phosphines)

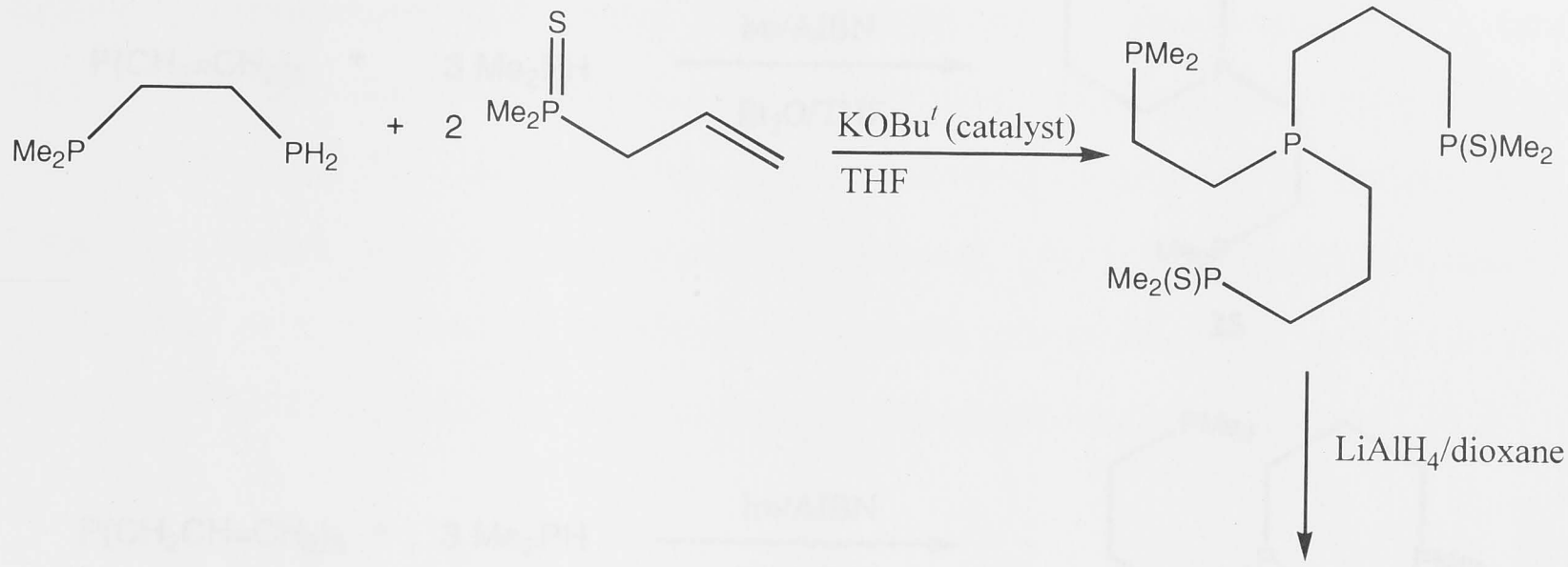
The first example of a tripodal tetra(tertiary phosphine) was tris(2-diphenylphosphinophenyl)phosphine (**19**), synthesised by Venanzi *et al.* in 1963 by reaction of $Li[C_6H_4PPh_2\text{-}2]$ and PCl_3 in THF, albeit in low yield.[67] A range of related ligands have since been prepared *via* several different routes. The most successful route, initially developed by King and Kapoor, has been the addition of a P-H moiety across the C=C moiety of a vinyl or allyl substituted tertiary phosphine. King and Kapoor synthesised tris(2-diphenylphosphinoethyl)phosphine (**20**) by the base-catalysed addition of three equivalents of diphenylphosphine to trivinylphosphine (Scheme 9).[68,69] Alternatively, **20** can be synthesised by bubbling phosphine, generated from the hydrolysis of aluminium phosphide, into a solution of diphenylvinylphosphine in THF containing a catalytic amount of potassium *tert*-butoxide (Scheme 9).[69]



20

Scheme 9

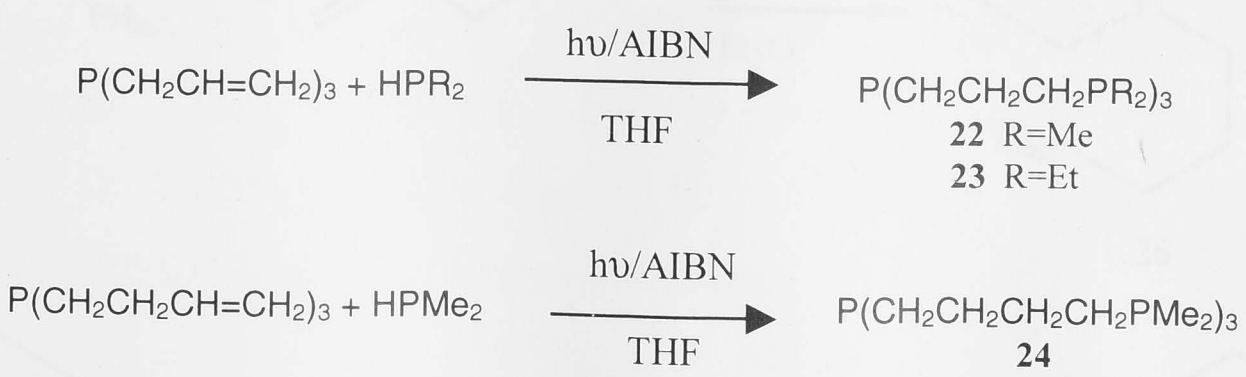
The tripodal ligand **21**, with terminal dimethylphosphino groups, has also been synthesised by King and co-workers, by the reaction of two equivalents of allyldimethylphosphine sulfide with (2-dimethylphosphinoethyl)phosphine, followed by desulfurisation with lithium aluminium hydride (Scheme 10). The yield of the desulfurisation step, however, was low due to the insolubility of the phosphine sulfide intermediate in organic solvents.[70]



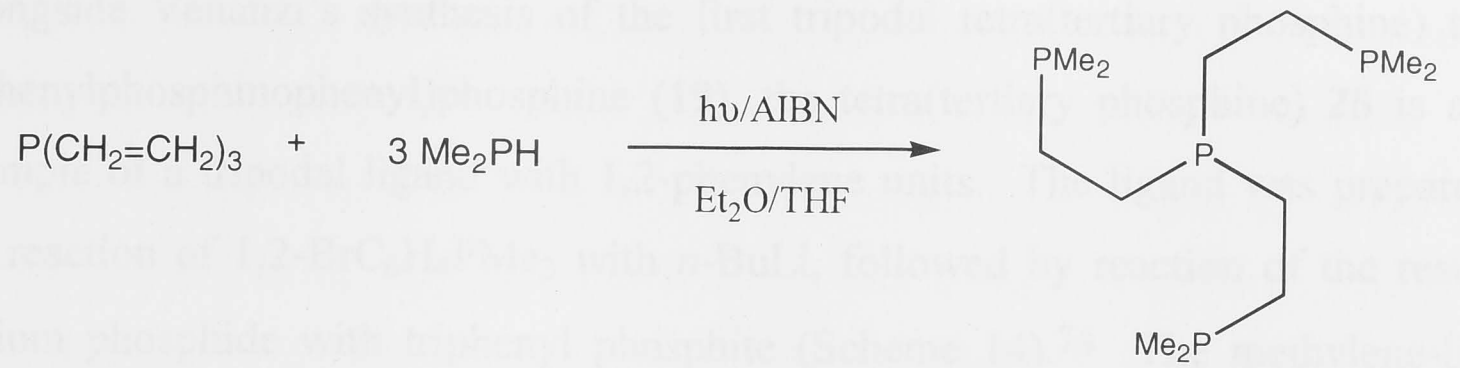
21

Scheme 10

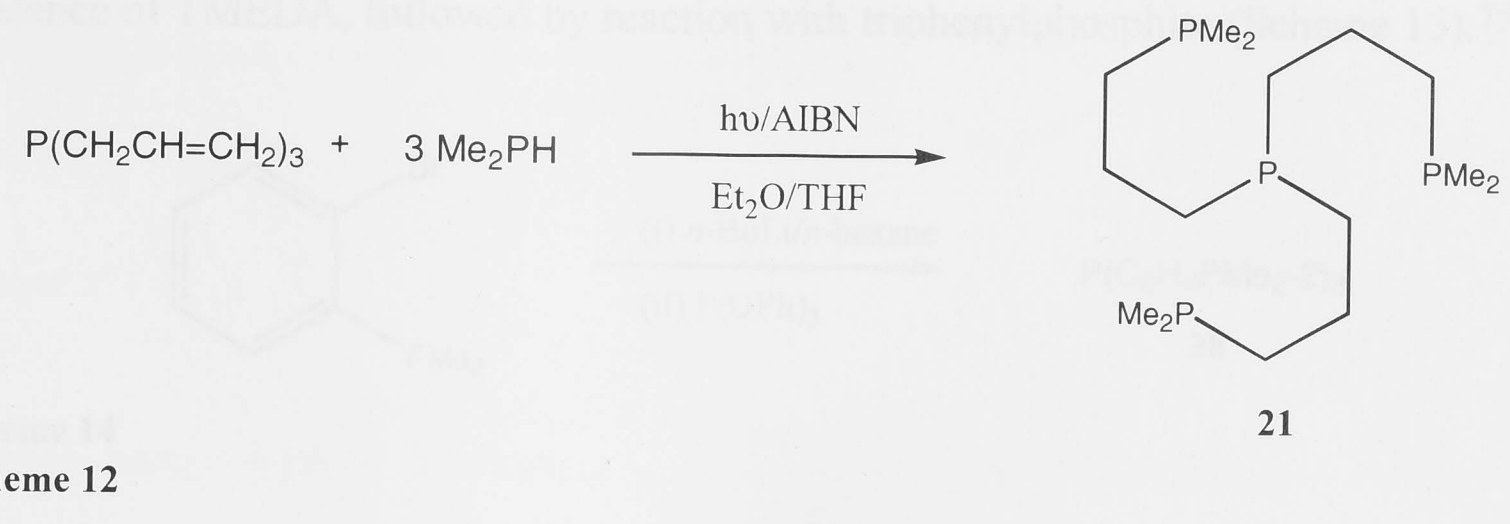
A similar methodology was used by Antberg *et al.*, except utilising UV/AIBN initiated free radical rather than base catalysed reactions. Consequently, longer and more flexible methylene chains, and terminal dimethyl- or diethyl- rather than diphenyl-phosphino groups, could be incorporated into these tripodal ligands, giving **22-24** (Scheme 11).[71,72]



Scheme 11



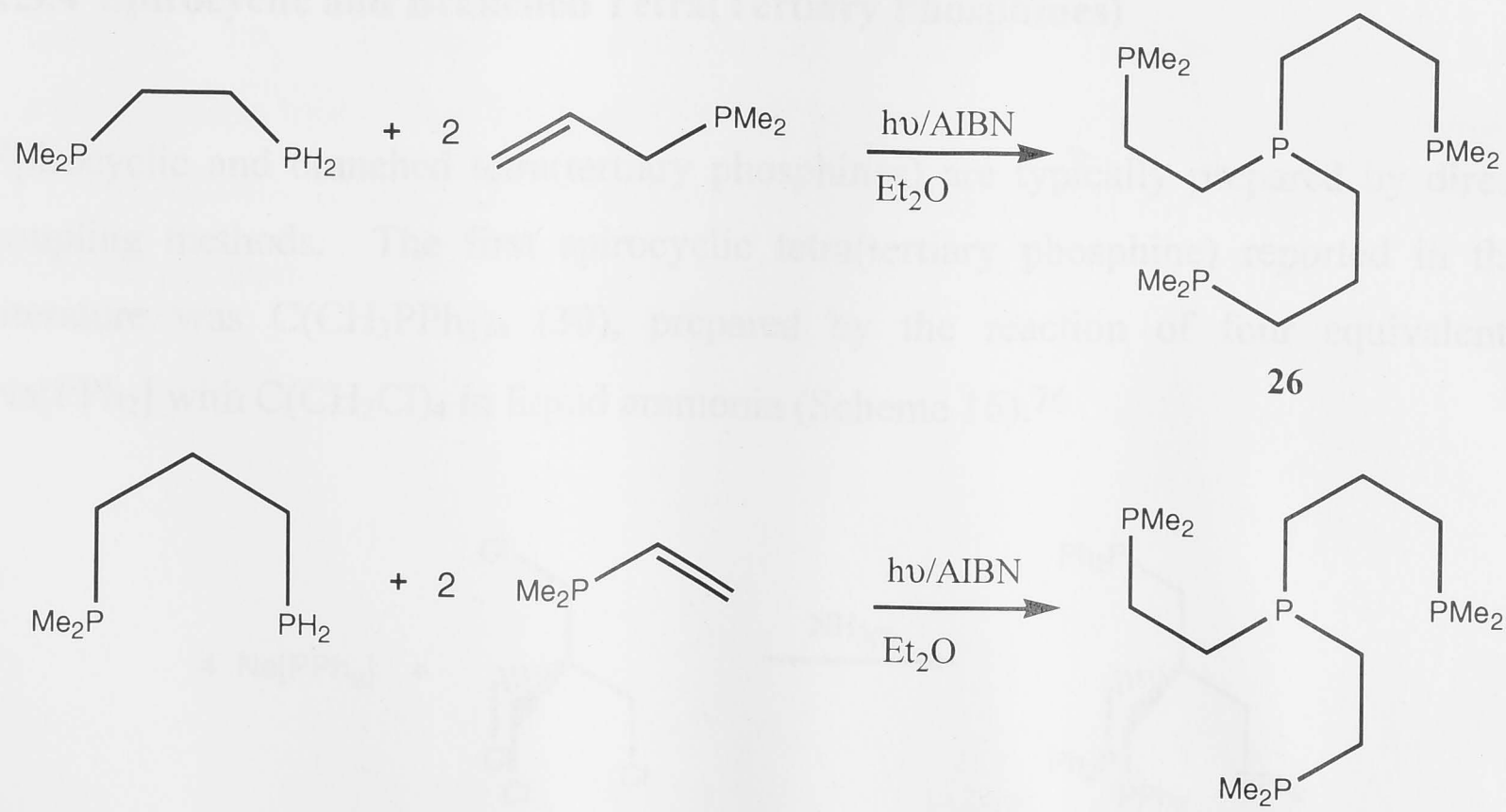
25



26

Scheme 12

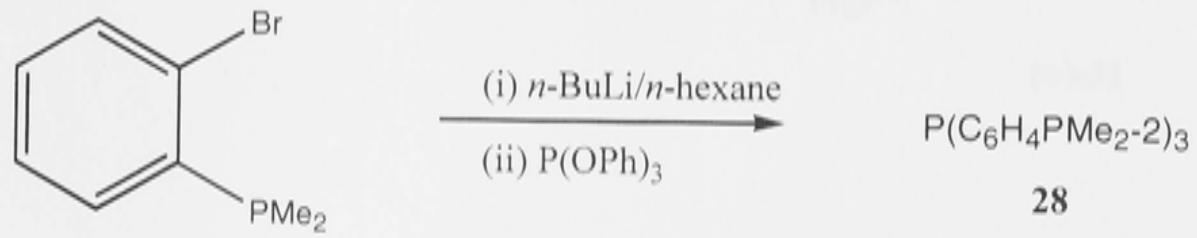
A number of related tripodal ligands were synthesised by Field and co-workers. The symmetrical tripodal tetra(tertiary phosphines) **25** and **21** were prepared in high yield, *via* the photochemical addition of dimethylphosphine across the vinyl or allyl groups of trivinyl- or triallyl-phosphine in the presence of AIBN (Scheme 12). A similar strategy was also utilised in the synthesis of the unsymmetrical tripodal ligands **26** and **27** (Scheme 13).[73]



27

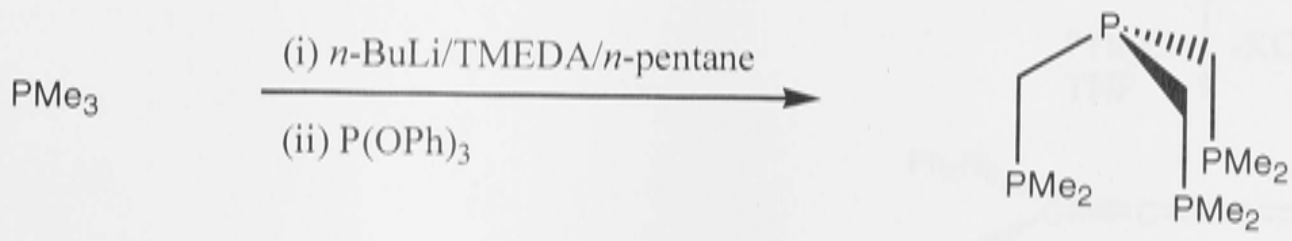
Scheme 13

Alongside Venanzi's synthesis of the first tripodal tetra(tertiary phosphine) tris(2-diphenylphosphinophenyl)phosphine (**19**), the tetra(tertiary phosphine) **28** is a rare example of a tripodal ligand with 1,2-phenylene units. The ligand was prepared by the reaction of 1,2-$BrC_6H_4PMe_2$ with *n*-BuLi, followed by reaction of the resulting lithium phosphide with triphenyl phosphite (Scheme 14).[74] The methylene-linked analogue **29** was obtained by metalation of trimethylphosphine using *n*-BuLi in the presence of TMEDA, followed by reaction with triphenylphosphite (Scheme 15).[75]



28

Scheme 14

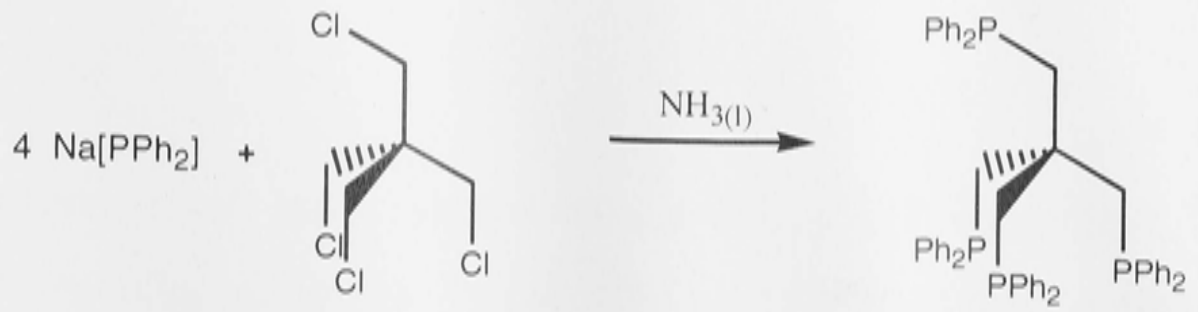


29

Scheme 15

1.3.4 Spirocyclic and Branched Tetra(Tertiary Phosphines)

Spirocyclic and branched tetra(tertiary phosphines) are typically prepared by direct coupling methods. The first spirocyclic tetra(tertiary phosphine) reported in the literature was $C(CH_2PPh_2)_4$ (**30**), prepared by the reaction of four equivalents $Na[PPh_2]$ with $C(CH_2Cl)_4$ in liquid ammonia (Scheme 16).[76]



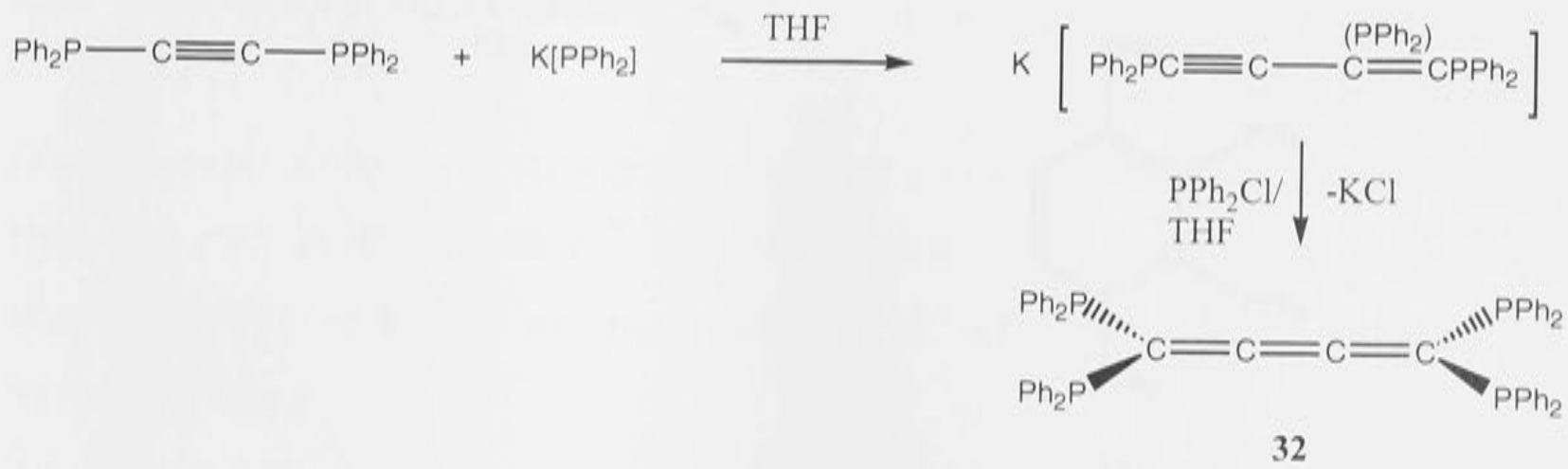
30

Scheme 16

The branched tetra(tertiary phosphine) (±)-**31** was synthesised by the metalation of 1-diphenylphosphinopropyne with *n*-BuLi and subsequent reaction with chlorodiphenylphosphine (Scheme 17).[77] The butatriene analogue **32** was prepared by reaction of bis(diphenylphosphino)ethyne with potassium diphenylphosphide in THF, followed by the addition of chlorodiphenylphosphine (Scheme 18).[78]

(±)-**31**

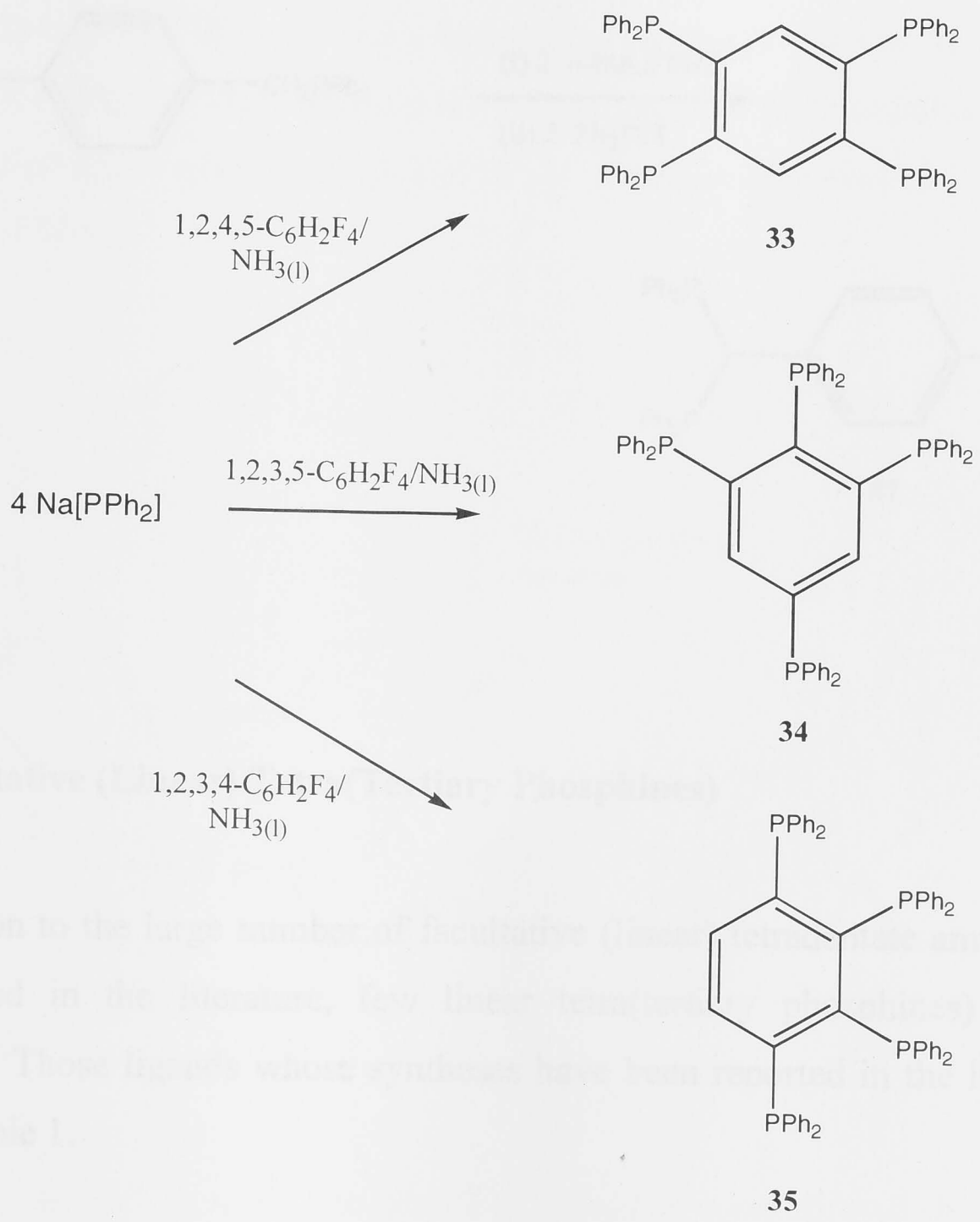
Scheme 17



32

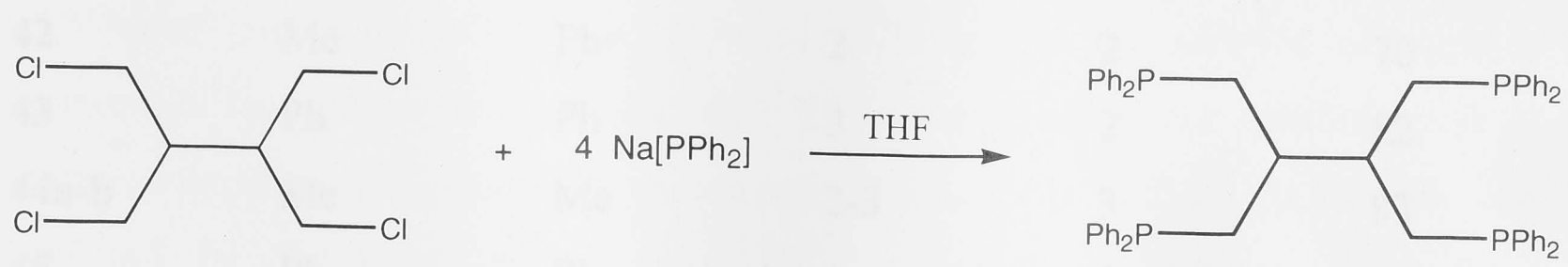
Scheme 18

McFarlane and co-workers made a number of polykis(diphenylphosphino)benzenes, including the tetra(tertiary phosphines) 1,2,3,4- 1,2,3,5- and 1,2,4,5-tetrakis(diphenylphosphino)benzene (**33-35**), by the direct coupling reaction between four equivalents of $Na[PPh_2]$ and the corresponding isomer of $C_6H_2F_4$, in liquid ammonia (Scheme 19).[79]



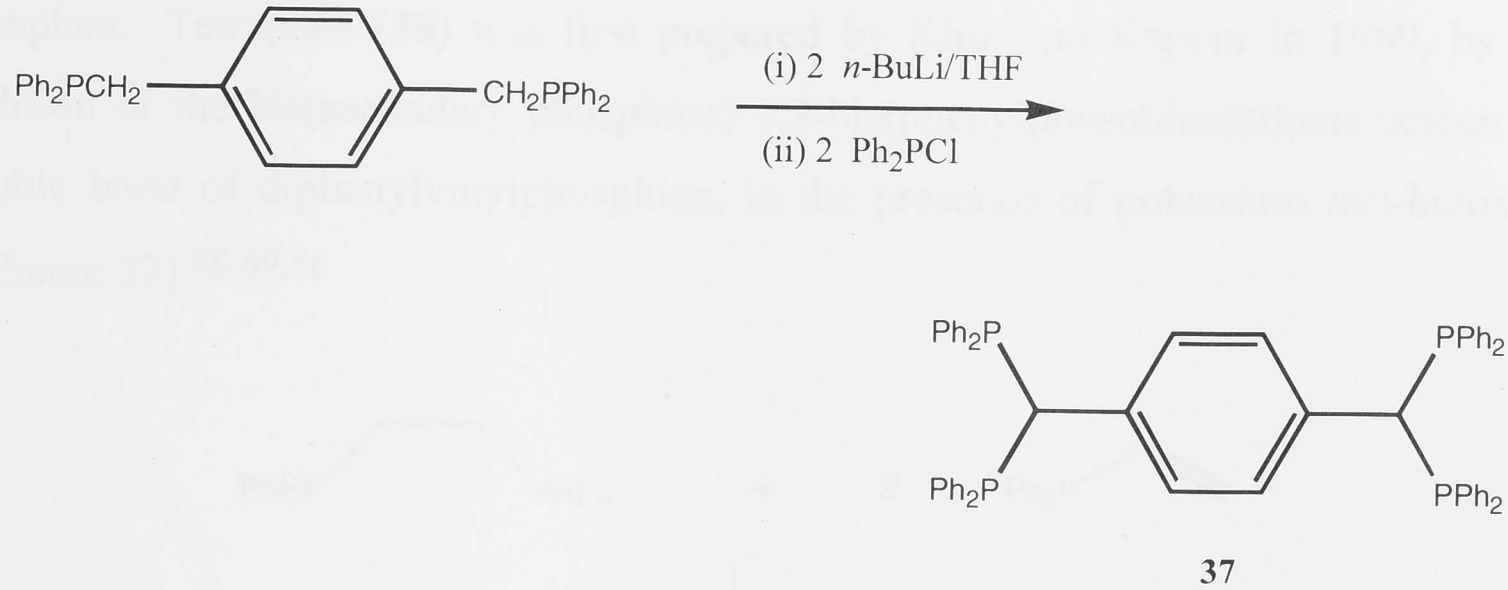
Scheme 19

Using a similar direct-coupling approach, Verkade and co-workers prepared the branched tetra(tertiary phosphine) **36** *via* reaction of four equivalents of $Na[PPh_2]$ with 2,3-bis(chloromethyl)-1,4-dichlorobutane in THF (Scheme 20).[80]



Scheme 20

Recently Barney *et al.* have synthesised $1,4\text{-}C_6H_4[CH(PPh_2)_2]_2$ (**37**) by stepwise addition of *n*-BuLi, followed by chlorodiphenylphosphine, to the di(tertiary phosphine) 1,4-bis(diphenylphosphinomethyl)benzene (Scheme 21).[81]



37

Scheme 21

1.3.5 Facultative (Linear) Tetra(Tertiary Phosphines)

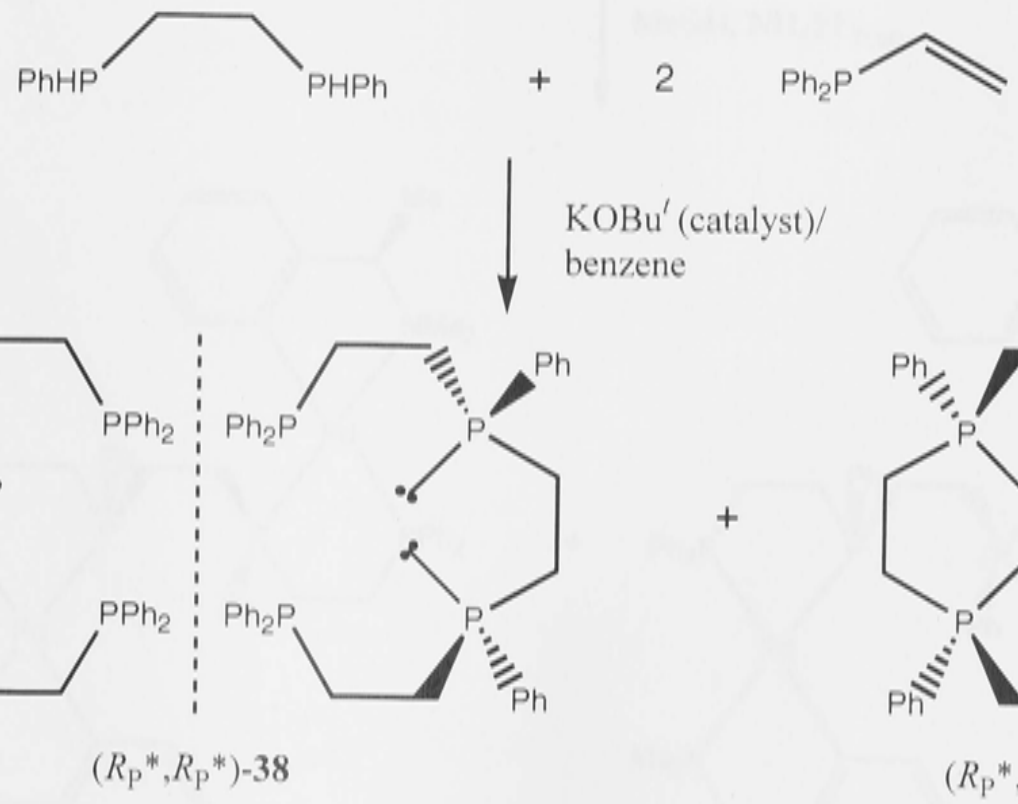
In comparison to the large number of facultative (linear) tetradentate amines to have been reported in the literature, few linear tetra(tertiary phosphines) have been synthesised. Those ligands whose syntheses have been reported in the literature are shown in Table 1.

Table 1 Linear Tetra(tertiary phosphines) of the type $R_2P(CH_2)_nP(R')(CH_2)_mP(R')(CH_2)_nPR_2$.

	R	R'	m	n	Reference
38	Ph	Ph	2	2	68
42	Me	Ph	2	2	70
43	Ph	Ph	3	2	82
44a-b	Me	Me	2-3	3	83
45	Ph	Ph	1	2	84
46	Et	Ph	1	2	84
49a-e	*i*-Pr	*i*-Pr	1-3, 6, 10	1	85
50	*i*-Pr	*i*-Pr	1	3	85

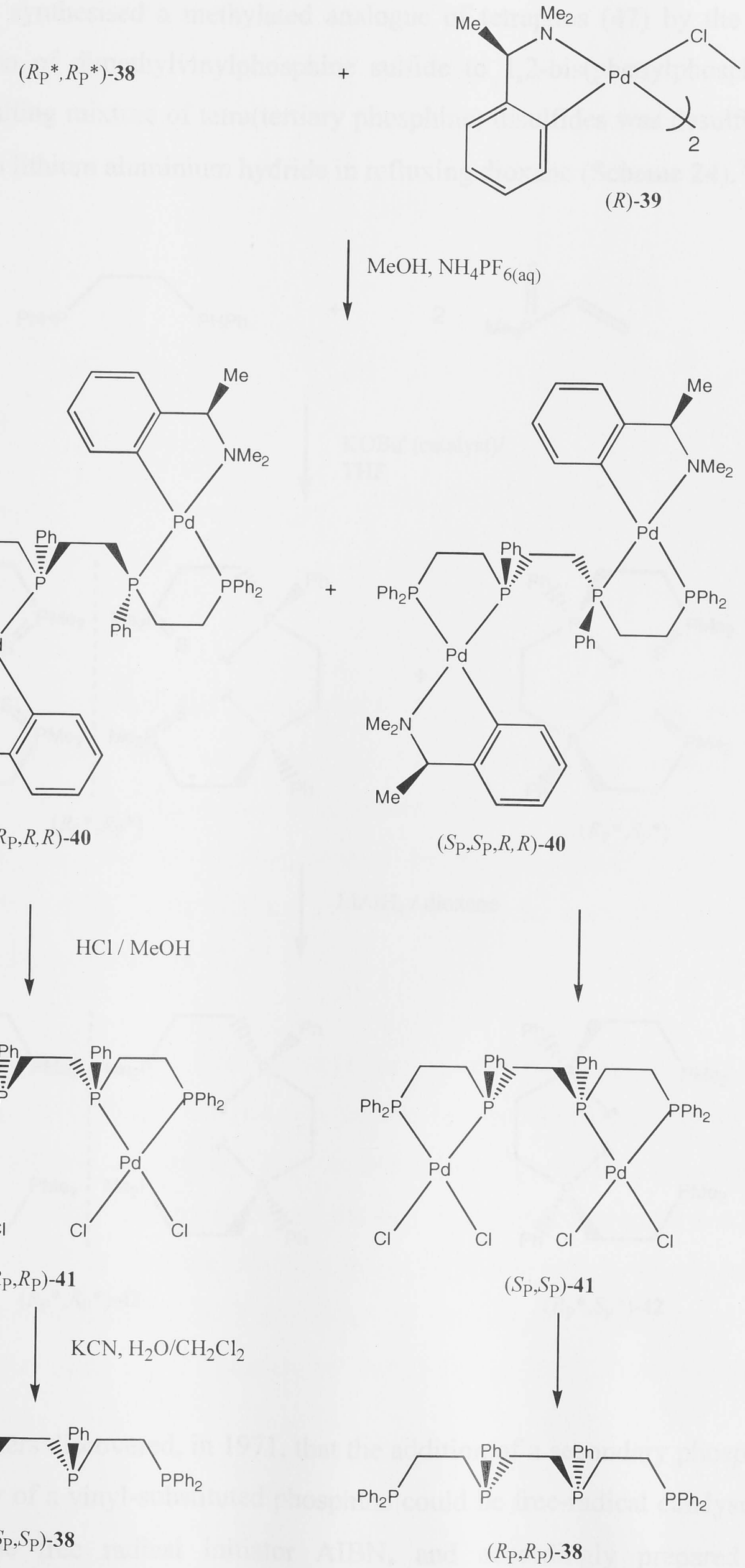
The best known and most widely studied of the linear tetra(tertiary phosphines) is 1,1,4,7,10,10-hexaphenyl-1,4,7,10-tetraphosphadecane (**38**), commonly known as

tetraphos. Tetraphos (**38**) was first prepared by King and Kapoor in 1969, by the addition of the bis(secondary phosphine) 1,2-bis(phenylphosphino)ethane across the double bond of diphenylvinylphosphine, in the presence of potassium *tert*-butoxide (Scheme 22).[68,69,86]



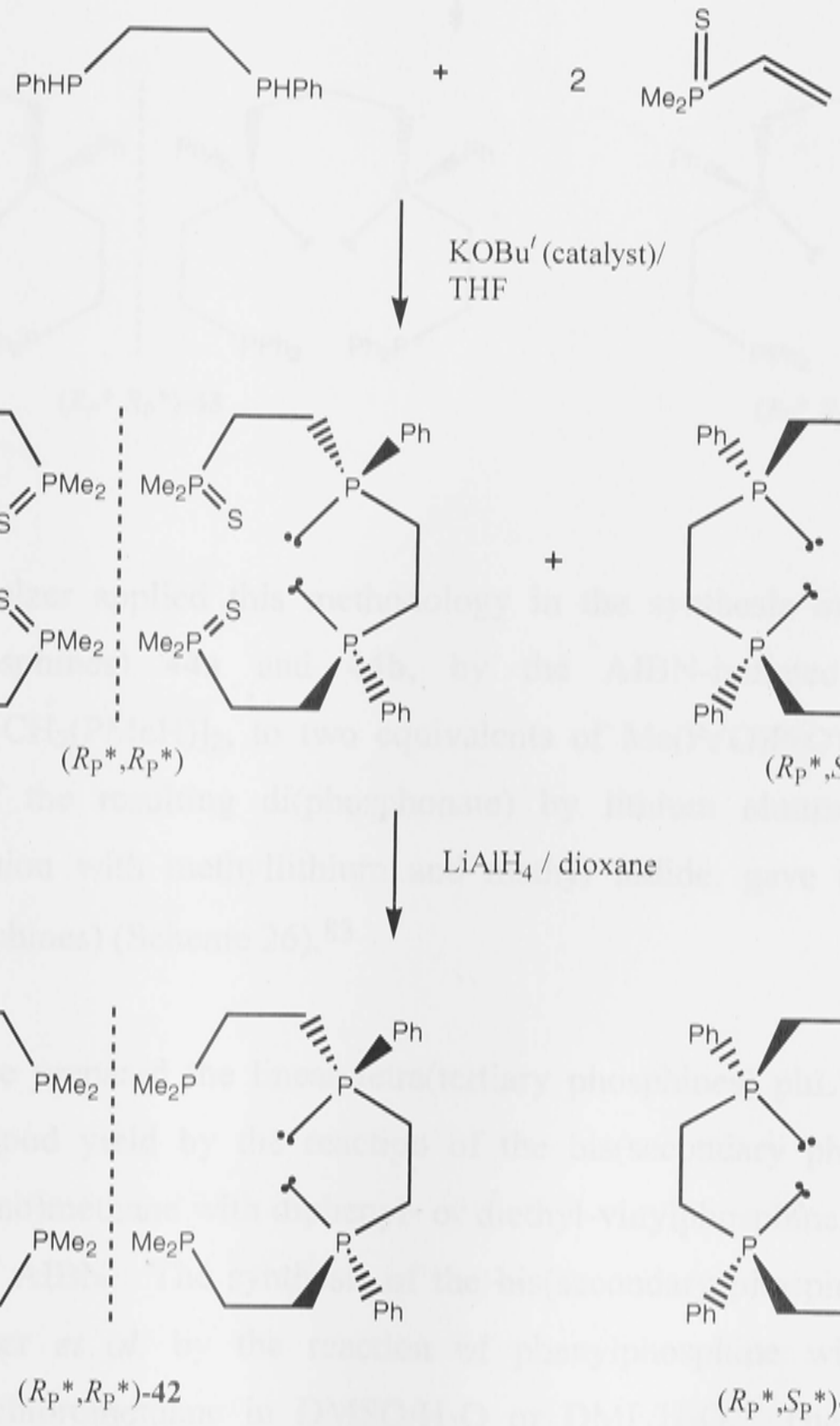
Scheme 22

Both the racemic and meso diastereomers of tetraphos were formed in the reaction, however, separation was achieved by selective extraction of (R_P*,R_P*)-**38** with tetrahydrofuran. The racemic diastereomer of **38** has also been resolved by the method of metal complexation. Diastereomeric bis[palladium(II)] complexes were prepared by reaction of equimolar amounts of (R_P*,R_P*)-**38** with the optically active palladium(II) dimer di-μ-chloro-bis{(*R*)-2-[1-(dimethylamino)ethyl]phenyl-C^1,N}dipalladium(II), [(*R*)-**39**] in methanol, followed by the addition of aqueous ammonium hexafluorophosphate (Scheme 23). Separation of the resulting pair of diastereomeric bis[palladium(II)] complexes (R_P,R_P,*R*,*R*)- and (S_P,S_P,*R*,*R*)-**40** was achieved by fractional crystallisation of the hexafluorophosphate salts from chloroform. Conversion of the separated diastereomers to the enantiomeric bis[dichloropalladium(II)] complexes, (R_P,R_P)- or (S_P,S_P)-**41**, followed by treatment with sodium cyanide, gave the optically pure ligands (R_P,R_P)- and (S_P,S_P)-tetraphos [(R_P,R_P)- and (S_P,S_P)-**38**].[87,88]


(R_P*,R_P*)-38
+
Me
Me2
N
Cl
Pd
2
(R)-39
MeOH, NH4PF6(aq)
Me
NMe2
Pd
Ph
Ph2P
P
P
PPh2
Ph
Pd
Me2N
Me
(R_P,R_P,R,R)-40
(S_P,S_P,R,R)-40
HCl / MeOH
Cl
Cl
Cl
Cl
(R_P,R_P)-41
(S_P,S_P)-41
KCN, H2O/CH2Cl2
(S_P,S_P)-38
(R_P,R_P)-38

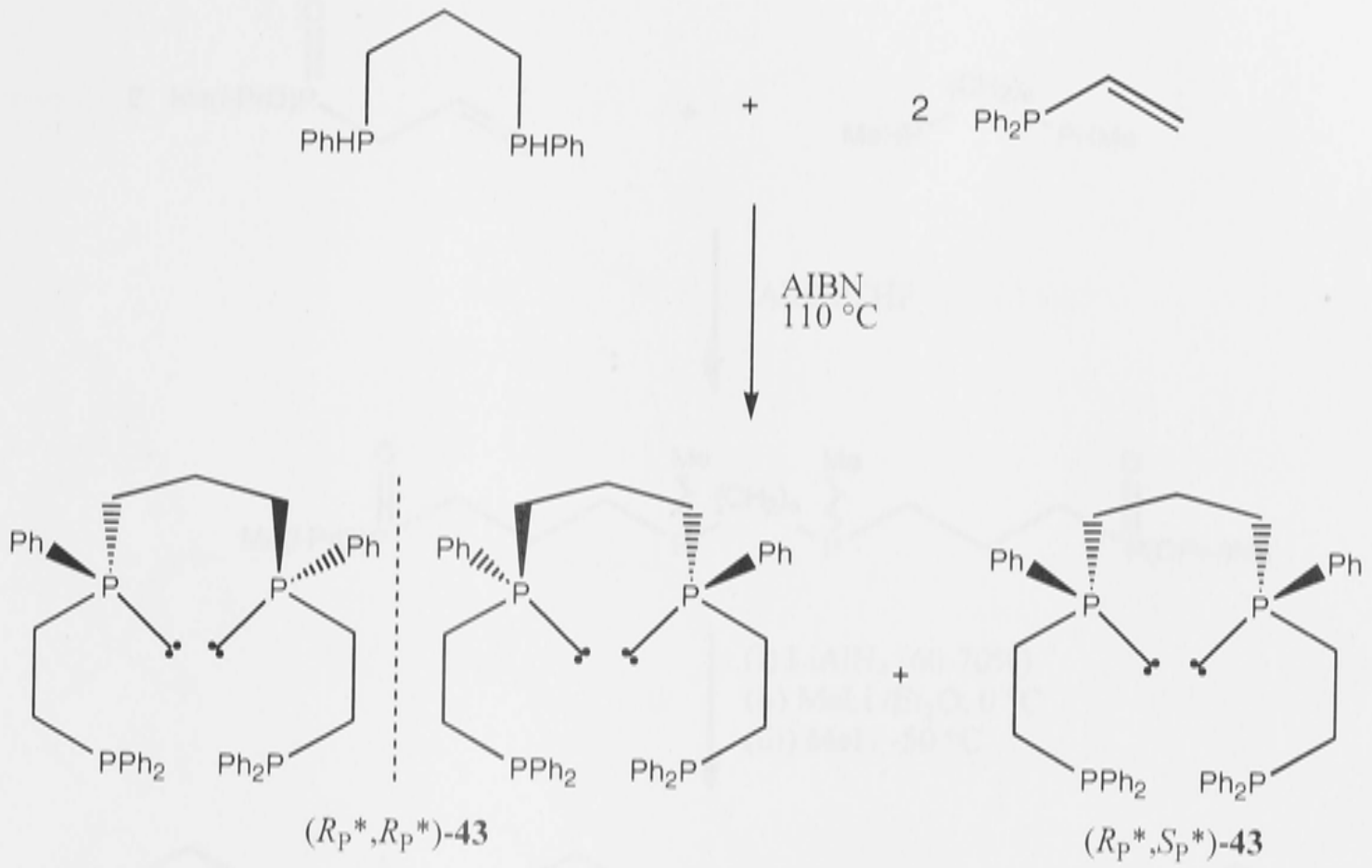
Scheme 23

King and Cloyd synthesised a methylated analogue of tetraphos (**42**) by the base-catalysed addition of dimethylvinylphosphine sulfide to 1,2-bis(phenylphosphino)-ethane. The resulting mixture of tetra(tertiary phosphine) disulfides was desulfurised by treatment with lithium aluminium hydride in refluxing dioxane (Scheme 24).[70]



Scheme 24

Meek and co-workers discovered, in 1971, that the addition of a secondary phosphine to the C=C moiety of a vinyl-substituted phosphine could be free-radical catalysed at 110 °C using the free radical initiator AIBN, and accordingly prepared the tetra(tertiary phosphine) (R_P*,R_P*)- and (R_P*,S_P*)-**43** (Scheme 25).[82]

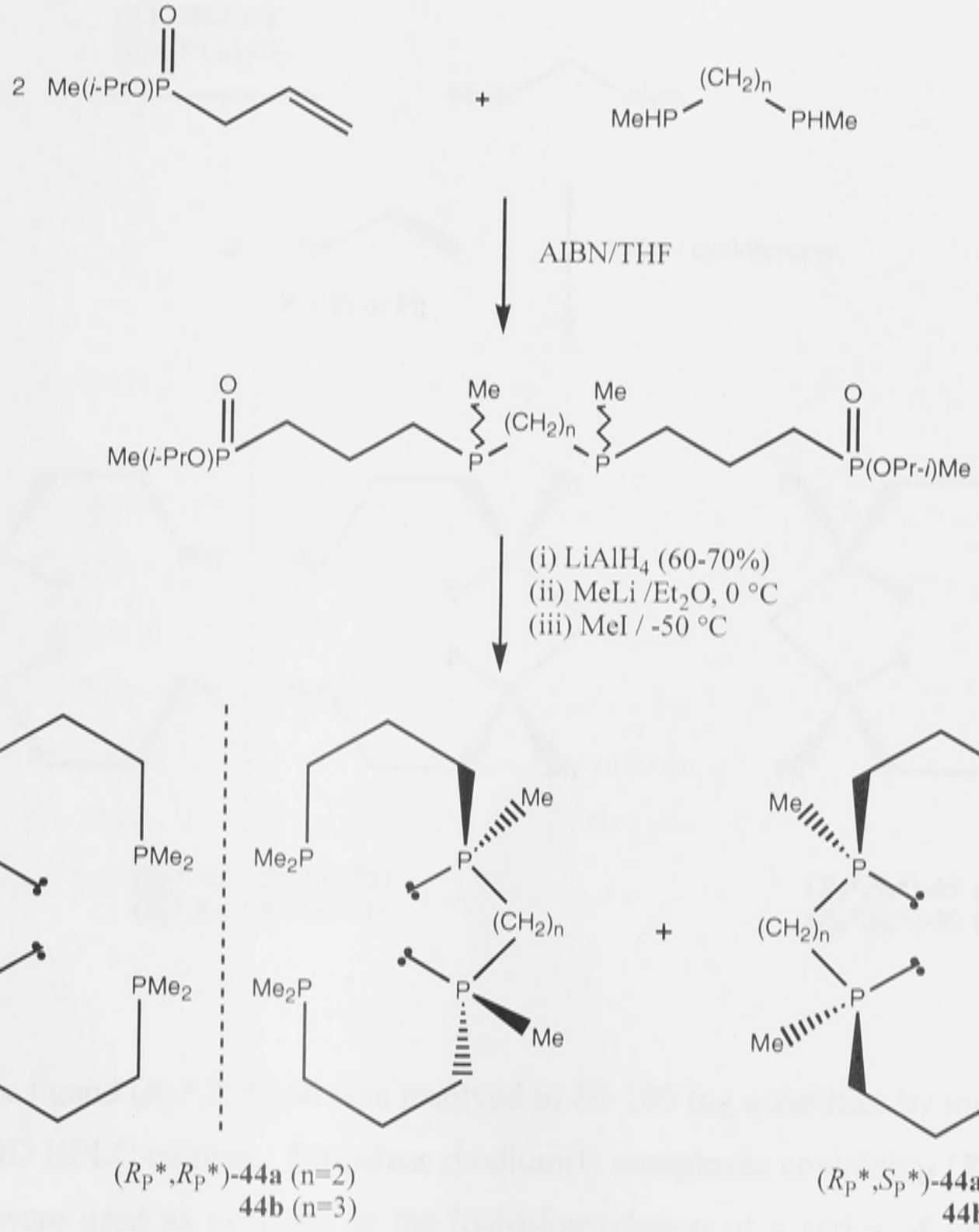


(R_P*,R_P*)-**43** (R_P*,S_P*)-**43**

Scheme 25

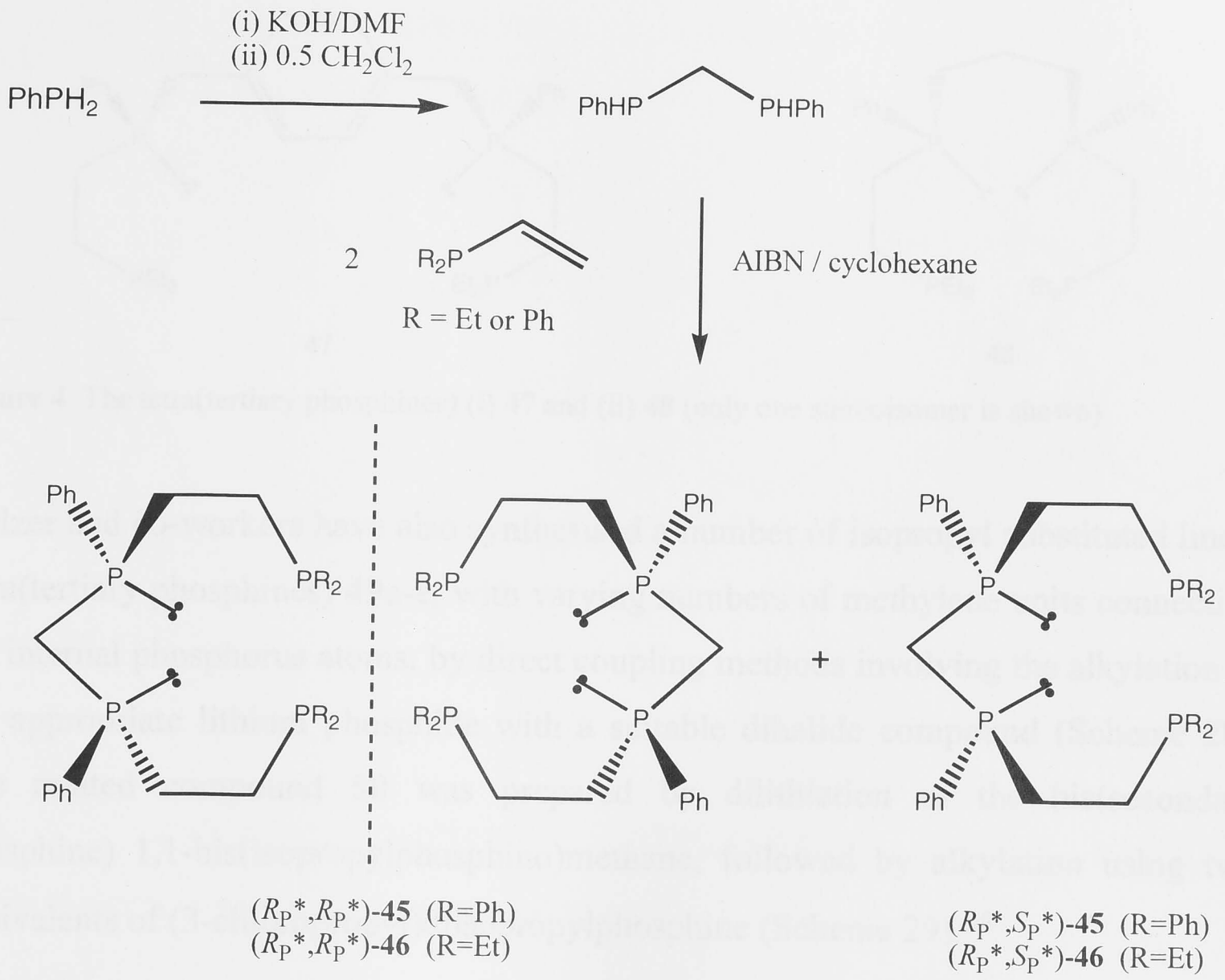
Hietkamp and Stelzer applied this methodology in the synthesis of the aliphatic tetra(tertiary phosphines) **44a** and **44b**, by the AIBN-initiated addition of $CH_2(PMeH)_2$ or $[CH_2(PMeH)]_2$, to two equivalents of $Me(Pr^iO)P(O)CH_2CH{=}CH_2$. The reduction of the resulting di(phosphonate) by lithium aluminium hydride, followed by reaction with methyllithium and methyl iodide, gave the respective tetra(tertiary phosphines) (Scheme 26).[83]

Stanley *et al.* have prepared the linear tetra(tertiary phosphines) phLTTP (**45**) and etLTTP (**46**) in good yield by the reaction of the bis(secondary phosphine) 1,2-bis(phenylphosphino)methane with diphenyl- or diethyl-vinylphosphine, respectively, in the presence of AIBN. The synthesis of the bis(secondary phosphine) was first reported by Stelzer *et al.* by the reaction of phenylphosphine with potassium hydroxide and dichloromethane in $DMSO/H_2O$ or DMF/H_2O. The tetra(tertiary phosphines) were generated as a 1:1 mixture of (R_P*,R_P*) and (R_P*,S_P*) diastereomers (Scheme 27).[84]



Scheme 26

The (R_P*,S_P*) diastereomer of **45** selectively crystallised from diethyl ether, to provide a viable method of separation of the two diastereomers. The (R_P*,R_P*) and (R_P*,S_P*) diastereomers of etLTTP (**46**) were separated by means of their binuclear square planar nickel(II) complexes. Although both diastereomeric complexes co-crystallised, the crystals of the complex containing the meso diastereomer quickly lost solvent upon standing and turned opaque, whilst the other isomer remained unchanged, allowing manual separation of the two diastereomeric complexes. The pair of diastereomeric nickel(II) complexes containing **46** could also be separated by column chromatography.[89]

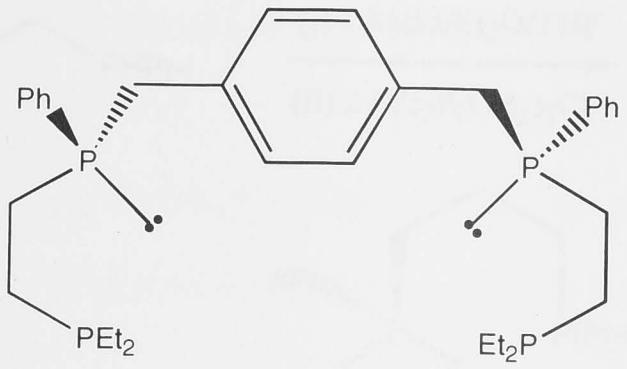


(R_P*,R_P*)-**45** (R=Ph)
(R_P*,R_P*)-**46** (R=Et)

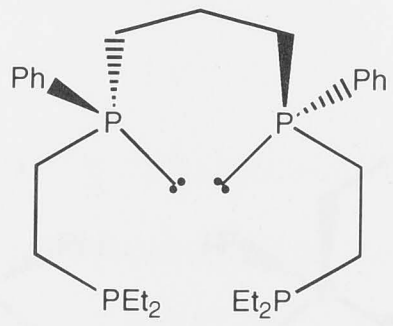
(R_P*,S_P*)-**45** (R=Ph)
(R_P*,S_P*)-**46** (R=Et)

Scheme 27

The racemic ligand (R_P*,R_P*)-**46** was resolved in 50-100 mg quantities by means of a Chiralcel OD HPLC column. Binuclear rhodium(I) complexes containing (R_P,R_P)- or (S_P,S_P)-**46** were used as catalysts in the hydroformylation of a series of vinyl ester substrates, with enantioselectivities as high as 85%.[90] A mechanism involving cooperativity between the two metal centres was proposed. To this end, Stanley and co-workers have also prepared the analogous quadridentate ligands **47** and **48** which have larger spacer groups between the two internal phosphorus atoms, thereby minimizing the scope for bimetallic cooperativity (Figure 4). As predicted, the binuclear rhodium(I) complexes of these ligands were found to be poor hydroformylation catalysts.[91] Again, both racemic and meso diastereomers of **47** and **48** were formed, but the synthetic routes to these ligands have not been reported.



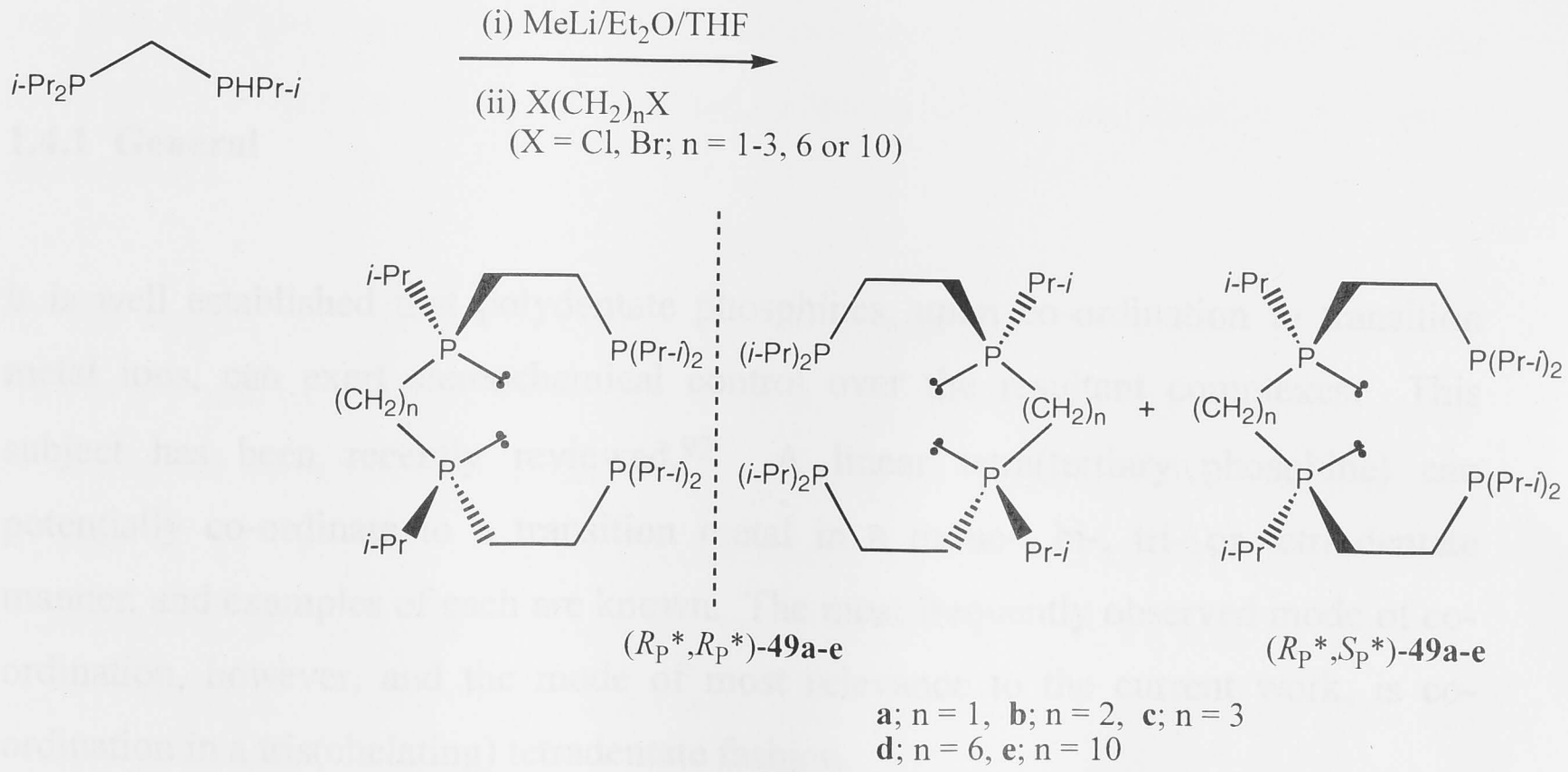
47



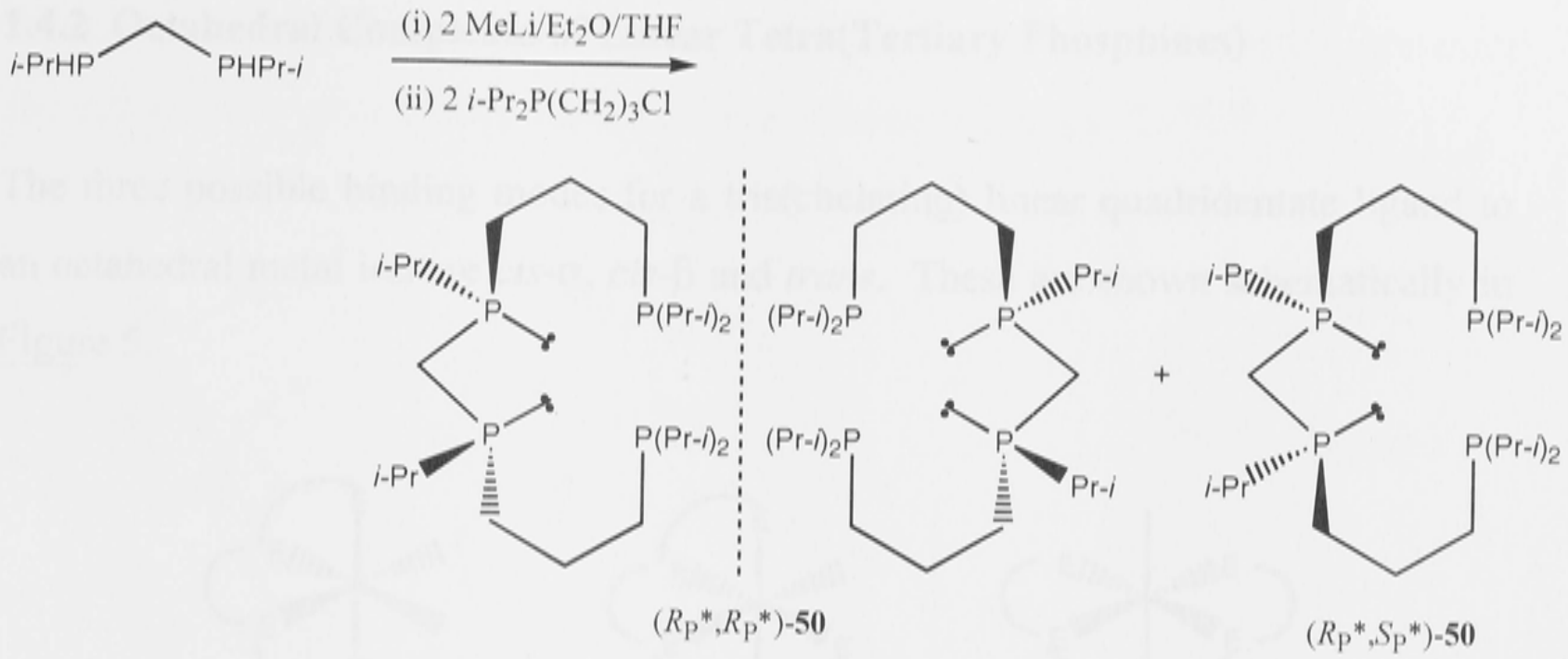
48

Figure 4 The tetra(tertiary phosphines) (i) **47** and (ii) **48** (only one stereoisomer is shown)

Stelzer and co-workers have also synthesised a number of isopropyl substituted linear tetra(tertiary phosphines) **49a-e**, with varying numbers of methylene units connecting the internal phosphorus atoms, by direct coupling methods involving the alkylation of the appropriate lithium phosphide with a suitable dihalide compound (Scheme 28). The related compound **50** was prepared by dilithiation of the bis(secondary phosphine) 1,1-bis(isopropylphosphino)methane, followed by alkylation using two equivalents of (3-chloropropyl)diisopropylphosphine (Scheme 29).[85]



Scheme 28



Scheme 29

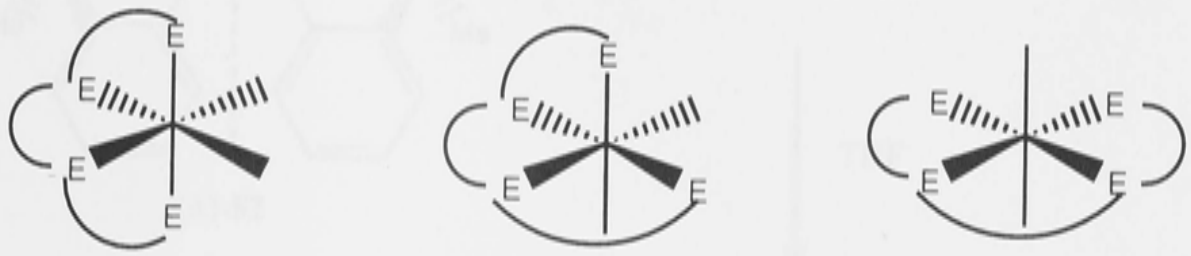
1.4 CO-ORDINATION CHEMISTRY OF LINEAR TETRA(TERTIARY PHOSPHINES)

1.4.1 General

It is well established that polydentate phosphines, upon co-ordination to transition metal ions, can exert stereochemical control over the resultant complexes. This subject has been recently reviewed.[92] A linear tetra(tertiary phosphine) can potentially co-ordinate to a transition metal in a mono-, bi-, tri- or tetra-dentate manner, and examples of each are known. The most frequently observed mode of co-ordination, however, and the mode of most relevance to the current work, is co-ordination in a tris(chelating) tetradentate fashion.

1.4.2 Octahedral Complexes of Linear Tetra(Tertiary Phosphines)

The three possible binding modes for a tris(chelating) linear quadridentate ligand to an octahedral metal ion are *cis*-α, *cis*-β and *trans*. These are shown schematically in Figure 5.



cis-α *cis*-β *trans*

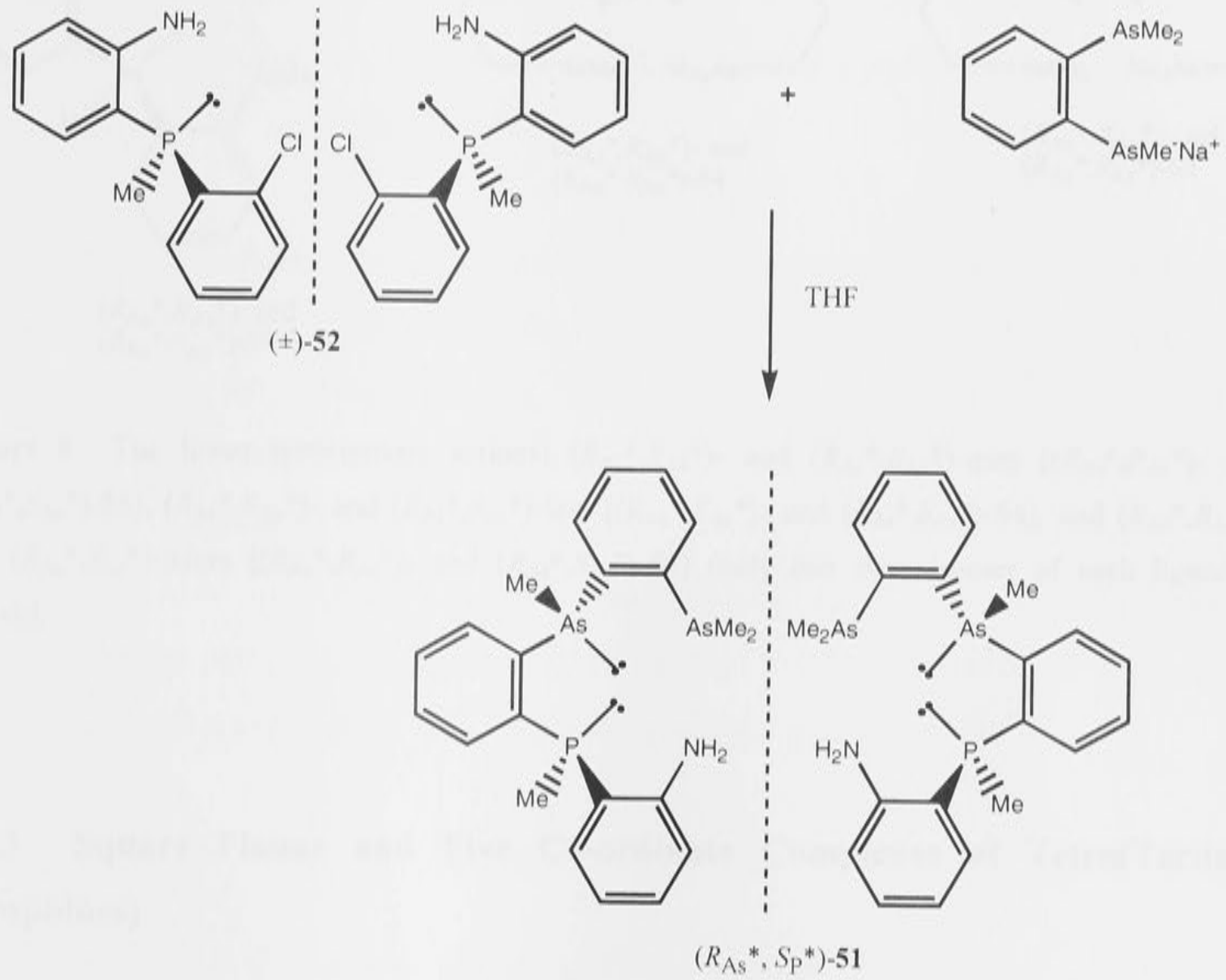
Figure 5 The three possible binding modes of a linear quadridentate ligand on an octahedral metal ion.

Five possible topological isomers are possible for the complexes of a linear quadridentate ligand containing two stereogenic donor atoms. The racemic diastereomer can form *cis*-α, *cis*-β and *trans* complexes, and the meso diastereomer can give *cis*-β and *trans* complexes, with the *cis*-α complex being inaccessible for the meso diastereomer due to the constrained geometry around the internal stereogenic donor atoms.

Of the known tetra(tertiary phosphines), the co-ordination chemistry of tetraphos [(R_P*,R_P*)- and (R_P*,S_P*)-**38**] has been the most extensively studied. A large number of octahedral complexes containing the diastereomeric forms of tetraphos have been reported in the literature. The *cis*-α diastereomer is preferentially formed upon co-ordination of (R_P*,R_P*)-**38** to octahedral transition metal ions (e.g Rh(III),[93] Fe(II), Os(II),[94] and Re(III)[95]) Both *cis*-β and *trans* complexes are formed upon co-ordination of the meso diastereomer (R_P*,S_P*)-**38** to these metals ions.

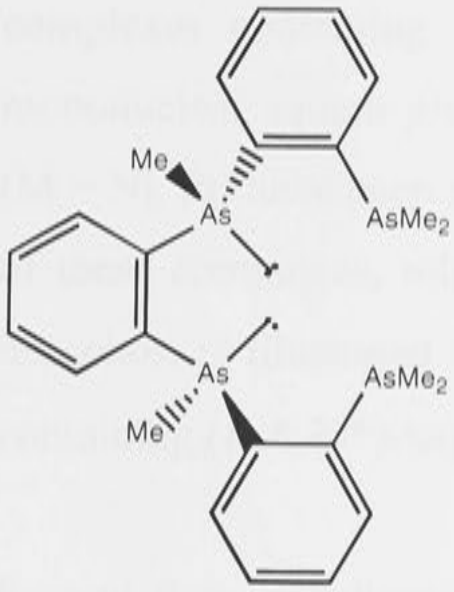
A similar result was observed for the related racemic linear quadridentate ligand (R_{As}*,S_P*)-**51**, with an As_2NP donor set. The quadridentate ligand (R_{As}*,S_P*)-**51** was synthesised in a completely stereoselective manner by the reaction of (±)-(2-aminophenyl)(2-chlorophenyl)methylphosphine (±)-**52** and sodium (2-dimethylarsino-phenyl)methylarsenide in THF (Scheme 30). The presence of three rigid 1,2-phenylene linkages in the ligand backbone is believed to be responsible for

the high stereoselectivity observed in the synthesis of (R_{As}*,S_P*)-**51** and the exclusive formation of the *cis*-α diastereomer on complexation to cobalt(III).[96,97]

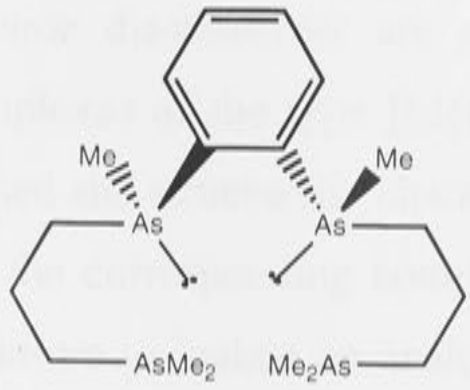


Scheme 30

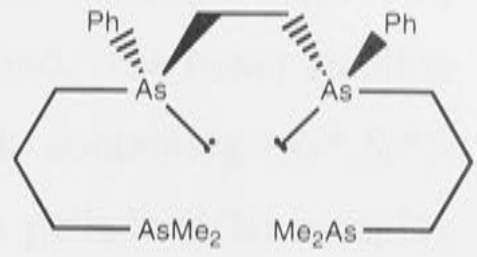
A related linear tetra(tertiary arsine) containing three 1,2-phenylene linkages, (R_{As}*,R_{As}*)-qars [(R_{As}*,R_{As}*)-**53**], was similarly found to form the *cis*-α diastereomer exclusively on co-ordination to cobalt(III). In contrast, the linear tetra(tertiary arsines) (R_{As}*,R_{As}*)- and (R_{As}*,S_{As}*)-fars [(R_{As}*,R_{As}*)- and (R_{As}*,S_{As}*)-**54**], and (R_{As}*,R_{As}*)- and (R_{As}*,S_{As}*)-tetars [(R_{As}*,R_{As}*)- and (R_{As}*,S_{As}*)-**55**], which contain flexible propylene chains between the terminal and internal arsenic donor atoms, formed all five possible topological isomers upon complexation to cobalt(III).[98-100] The three tetra(tertiary arsines) are shown in Figure 6. Fractional crystallisation of the isomeric complexes lead to separation of the racemic and meso diastereomers of the three tetra(tertiary arsines). Of these three ligands only (R_{As}*,R_{As}*)-**54** has been resolved, *via* the separation by fractional crystallisation of a pair of diastereomeric cobalt(III) D-(-)-dibenzoyl hydrogen tartrate salts containing the ligand.[99]



(R_{As}*,R_{As}*)- and
(R_{As}*,S_{As}*)-**53**



(R_{As}*,R_{As}*)- and
(R_{As}*,S_{As}*)-**54**



(R_{As}*,R_{As}*)- and
(R_{As}*,S_{As}*)-**55**

Figure 6 The linear tetra(tertiary arsines) (R_{As}*,R_{As}*)- and (R_{As}*,R_{As}*)-qars [(R_{As}*,R_{As}*)- and (R_{As}*,S_{As}*)-**53**], (R_{As}*,R_{As}*)- and (R_{As}*,S_{As}*)-fars [(R_{As}*,R_{As}*)- and (R_{As}*,S_{As}*)-**54**], and (R_{As}*,R_{As}*)- and (R_{As}*,S_{As}*)-tetars [(R_{As}*,R_{As}*)- and (R_{As}*,S_{As}*)-**55**] (only one stereoisomer of each ligand is shown).

1.4.3 Square Planar and Five Co-ordinate Complexes of Tetra(Tertiary Phosphines)

There has been much interest in square planar and five-coordinate complexes containing tetra(tertiary phosphines), largely because they can give rise to structures that cannot be anticipated with di(tertiary phosphines), and have potential applications as chiral auxiliaries in homogenous catalysis.[21] Stanley and co-workers have characterised a number of binuclear square planar complexes of nickel(II) and rhodium(I) containing the tetra(tertiary phosphine) (R_P*,R_P*)- and (R_P*,S_P*)-**46**.[89] Similarly, a number of binuclear nickel(II), palladium(II), platinum(II)[101,102] and rhodium(I)[93] complexes containing the diastereomeric forms of tetraphos [(R_P*,R_P*)- and (R_P*,S_P*)-**38**] have also been prepared.

Mononuclear square planar complexes containing linear tetra(tertiary phosphines) are less numerous in the literature and typically contain the meso diastereomer of the ligand. For example, the complex ions [M{(R_P*,S_P*)-tetraphos}]$^+$ (M = Ir, Rh)[93,103] and [M{(R_P*,S_P*)-tetraphos}]$^{2+}$ (M = Ni, Pd, Pt) have been reported. Related

complexes containing the racemic diastereomer are also known. For example, mononuclear square planar complexes of the type [M{(R_P*,R_P*)-tetraphos}]$(BPh_4)_2$ (M = Ni, Pt) have been synthesised and structurally characterised. The lower stability of these complexes, relative to the corresponding compounds containing (R_P*,S_P*)-tetraphos, is illustrated by the failure to isolate an analogous palladium(II) complex containing (R_P*,R_P*)-tetraphos.[104,105]

Several five-co-ordinate complexes containing linear tetra(tertiary phosphines) have been prepared although relatively few have been structurally characterised. The complex [FeBr{(R_P*,R_P*)-tetraphos}]$^+$ is one of the few complexes of this type to have been structurally characterised and was shown to have a distorted trigonal bipyramidal geometry.[106] Similar complexes of nickel(II), palladium(II) and platinum(II) have also been prepared and typically have a trigonal bipyramidal geometry. The complex, [PtCl{(R_P*,S_P*)tetraphos}](BPh_4), however, is an example of a five co-ordinate complex with a square pyramidal geometry.[107]

1.4.4 Tetrahedral Complexes of Linear Tetra(Tertiary Phosphines)

Wild and co-workers recently observed that the enantiomers of tetraphos [(R_P,R_P)- and (S_P,S_P)-**38**] spontaneously assembled into homochiral, double-stranded disilver(I) and digold(I) helicates of the type $[M_2(tetraphos)_2]X_2$, when reacted with the appropriate silver(I) and gold(I) salts. In each case the geometry around the metal ions was tetrahedral. The disilver(I) complex of (S_P,S_P)-**38** was found to form both a left-handed D_2-double helix structure, and a C_2-side-by-side helix conformation, whereas the digold(I) complex was found to form only the side-by-side helix. Examples of each type are shown in Figure 7.[88]

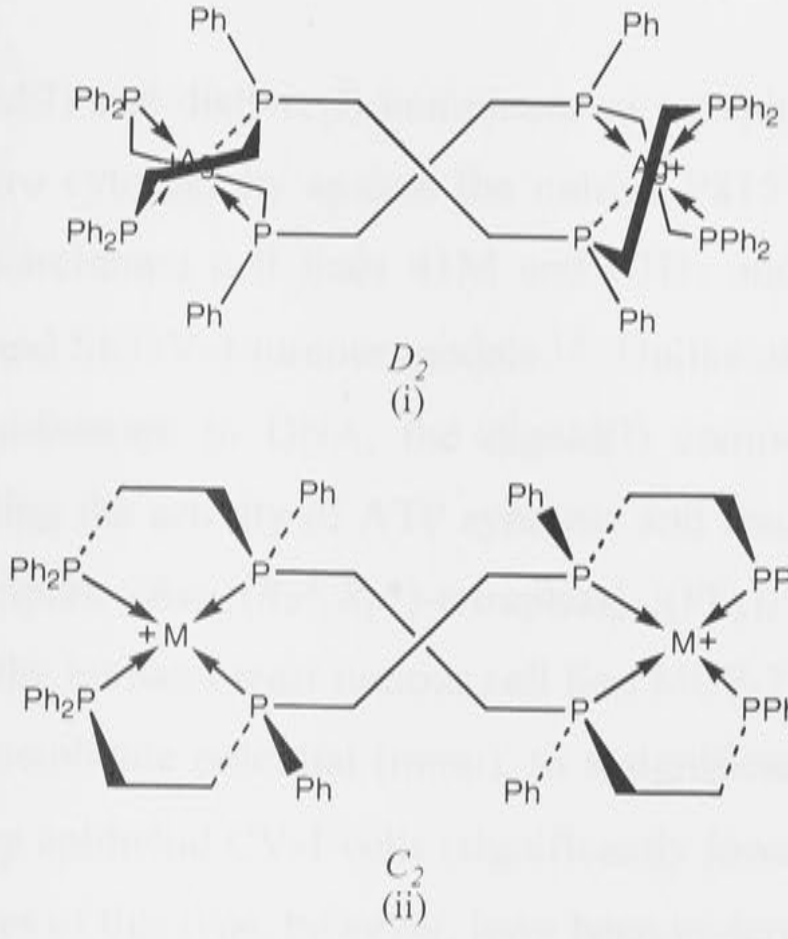


Figure 7 Bimetallic helicates of tetraphos: (i) The D_2-double helix of Λ-$[Ag_2\{(R_P,R_P)$-tetraphos$\}]^{2+}$, and (ii) C_2-side-by-side helix of Λ-$[M_2\{(R_P,R_P)$-tetraphos$\}]^{2+}$ (M=Ag, Au).

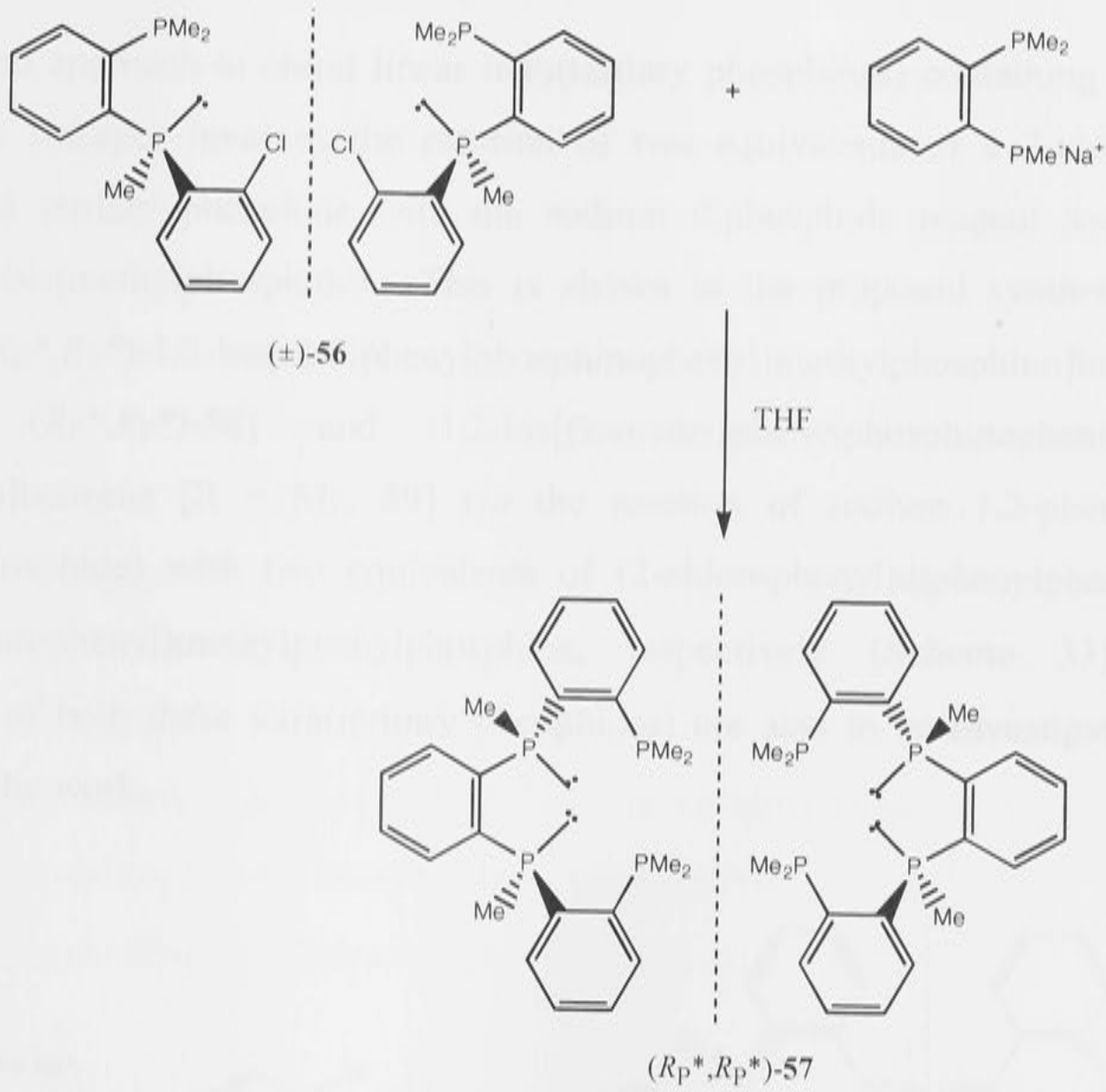
Tetraphos has also been found to form a binuclear, tetrahedral platinum(0)[108] complex and a mononuclear tetrahedral complex with copper(I),[88] but no report of a mononuclear silver(I) or gold(I) complex containing a tetra(tertiary phosphine) has appeared in the literature. Several gold(I) complexes of the formula [Au(tetraphos)]X (X = halogen, thiosugar) have been patented by SmithKline Beckman Corp., USA, as antitumour agents,[109] although no information on their synthesis or structural data has been published.

Attention has recently focused on the antiproliferative properties of tetrahedral gold(I), silver(I) and copper(I) complexes containing multidentate tertiary phosphines. Most of the studies to date have focused on complexes containing the di(tertiary phosphine) 1,2-bis(diphenylphosphino)ethane (dppe) and in particular $[Au(dppe)_2]Cl$, which has shown both *in vitro* and *in vivo* activity comparable to that of the highly successful platinum anti-cancer drug cisplatin *cis*-$[PtCl_2(NH_3)_2]$ against a range of murine tumour cell lines, as well as activity against certain cisplatin resistant ovarian tumour cell lines. The complex, however, was subsequently shown to be too toxic for clinical use due to side-effects related to the disruption of mitochondrial function in hepatocytes, and acute cardiotoxicity in dogs.[11,110]

More recently, digold(I) and disilver(I) complexes of tetraphos have been shown to exhibit similar *in vitro* cytotoxicity against the murine P815 mastocytoma cell line; the human ovarian carcinoma cell lines 41M and CH1; and the cisplatin resistant 41McisR, CH1cisR and SKOV-3 tumour models.[13] Unlike cisplatin, whose mode of action involves co-ordination to DNA, the digold(I) compounds appear to target mitochondria, inhibiting the activity of ATP synthase and leading to rapid cell death. Importantly, the complex $[Au_2\{(R_P^*,R_P^*)\text{-tetraphos}\}_2](PF_6)_2$ was shown to inhibit colony formation of the human breast tumour cell line MCF-7, which has a relatively high mitochondrial membrane potential (mmp), to a significantly greater extent than that of monkey kidney epithelial CV-1 cells (significantly lower mmp).[111] No *in vivo* studies with complexes of this type, however, have been undertaken to date.

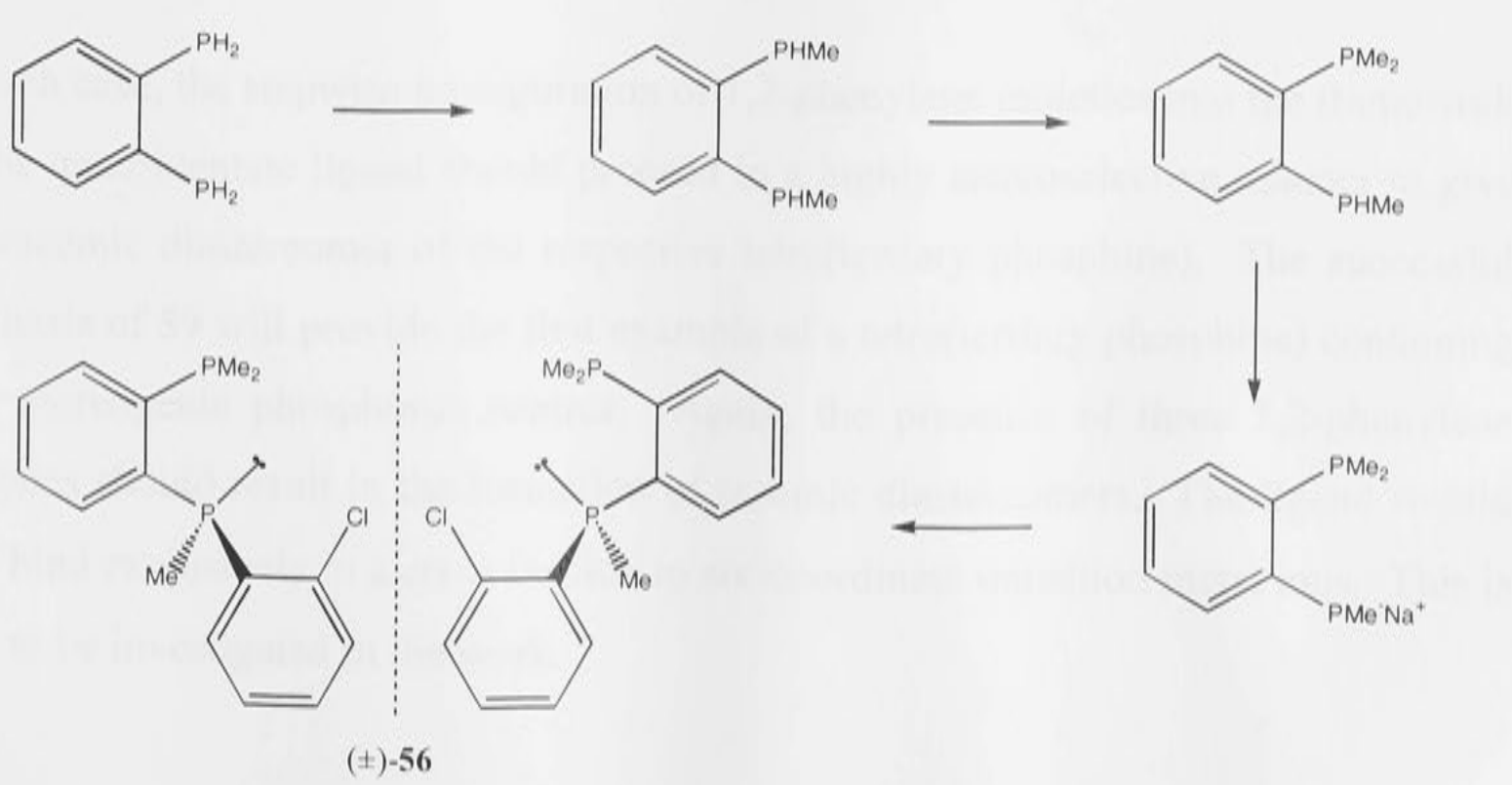
1.5 AIM

The aim of the work is to devise a viable synthetic route to chiral linear tetra(tertiary phosphines) containing three 1,2-phenylene linkages. Two approaches towards the synthesis of these tetra(tertiary phosphines) are to be investigated during the course of the work, both of which feature the stepwise coupling of 1,2-phenylene substituted precursors. The first approach involves the formation of a 2-chlorophenyl substituted di(tertiary phosphine) from 1,2-dichlorobenzene and an appropriately substituted sodium phosphide reagent, followed by further reaction of the 2-chlorophenyl substituted product with a second equivalent of the phosphide reagent, as shown by the reaction of (±)-(2-chlorophenyl)(2-dimethylphosphinophenyl)methylphosphine [(±)-**56**] with sodium (2-dimethylphosphinophenyl)methylphosphide to give (R_P^*,R_P^*)-1,2-bis[(2-dimethylphosphinophenyl)methylphosphino]benzene [(R_P^*,R_P^*)-**57**] (Scheme 31). The synthesis of the tetra(tertiary phosphine) [(R_P^*,R_P^*)-**57**] is to be investigated in the course of the work.



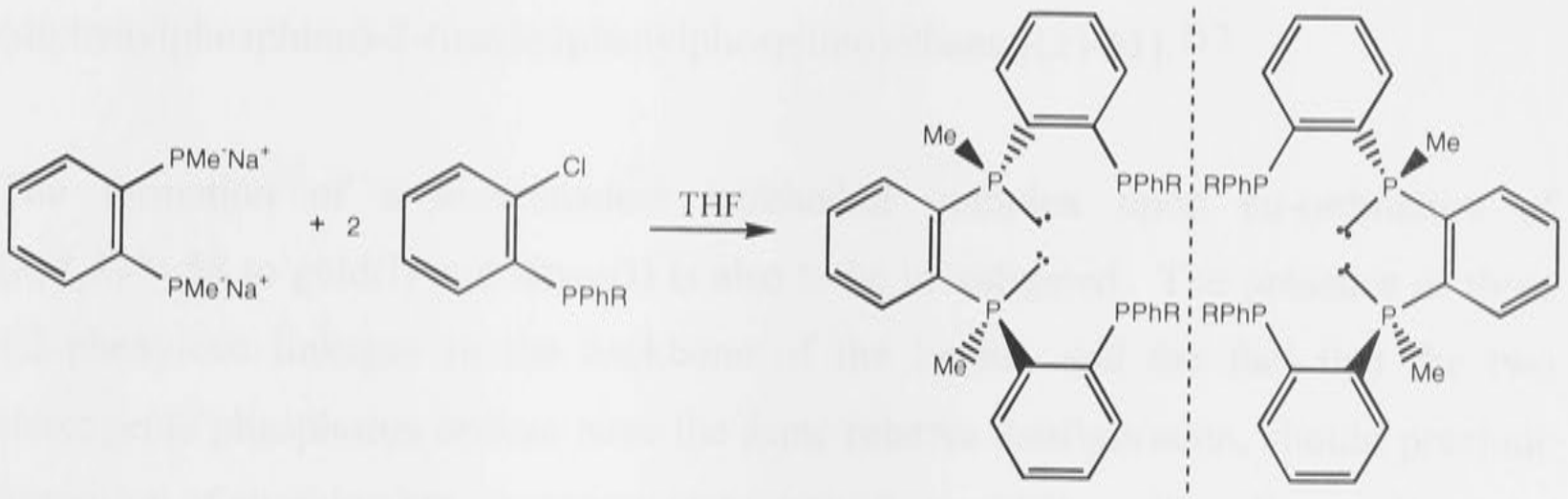
Scheme 31

The proposed synthetic route to the precursor (±)-(2-chlorophenyl)(2-dimethylphosphinophenyl)methylphosphine [(±)-**56**] is shown schematically in Scheme 32, and involves the stepwise methylation of the bis(primary phosphine) 1,2-phenylenebis(phosphine).



Scheme 32

The second approach to chiral linear tetra(tertiary phosphines) containing three 1,2-phenylene linkages involves the reaction of two equivalents of a 2-chlorophenyl substituted tertiary phosphine with the sodium diphosphide reagent sodium 1,2-phenylenebis(methylphosphide). This is shown in the proposed syntheses of the ligands (R_P*,R_P*)-1,2-bis[(2-diphenylphosphinophenyl)methylphosphino]benzene [R = Ph, (R_P*,R_P*)-**58**] and 1,2-bis[(2-methylphenylphosphinophenyl)methyl-phosphino]benzene [R = Me, **59**] *via* the reaction of sodium 1,2-phenylenebis-(methylphosphide) with two equivalents of (2-chlorophenyl)diphenylphosphine or (±)-(2-chlorophenyl)methylphenylphosphine, respectively (Scheme 33). The syntheses of both these tetra(tertiary phosphines) are also to be investigated in the course of the work.



(R_P*,R_P*)-**58** (R=Ph)
(R_P*,R_P*)-**59** (R=Me)

Scheme 33

In each case, the stepwise incorporation of 1,2-phenylene moieties into the framework of the quadridentate ligand should proceed in a highly stereoselective manner to give the racemic diastereomer of the respective tetra(tertiary phosphine). The successful synthesis of **59** will provide the first example of a tetra(tertiary phosphine) containing four stereogenic phosphorus centres. Again, the presence of three 1,2-phenylene moieties should result in the formation of racemic diastereomers. The ligand should also bind exclusively in a *cis*-α fashion to six-coordinate transition metal ions. This is also to be investigated in the work.

The presence of methyl substituents on the internal phosphorus stereocentres will be a useful tool in the stereochemical identification of the ligand and, in particular, its transition metal complexes, by ^{1}H NMR spectroscopy. The presence of both alkyl and aryl groups on a stereogenic phosphorus (or arsenic) atom can also be beneficial when effecting a resolution of the racemic tertiary phosphine (or arsine). Most resolution procedures rely on the separation by fractional crystallisation of a pair of diastereomers containing the tertiary phosphine and an optically active agent. The resolution of (±)-(2-chlorophenyl)(2-dimethylphosphinophenyl)methylphosphine and the tetra(tertairy phosphine) (R_P*,R_P*)-**58** *via* the method of metal complexation is to be investigated in the work. Successful resolutions have previously been effected for the (2-chlorophenyl) substituted bidentate ligand (±)-(2-aminophenyl)(2-chlorophenyl)methylphosphine [(±)-**52**][97] and the asymmetric di(tertiary phosphines) (±)-1-(diphenylphosphino)-2-(methylphenylphosphino)benzene [(±)-**60**][112] and (±)-1-(diphenylphosphino)-2-(methylphenylphosphino)ethane [(±)-**61**].[113]

The formation of a mononuclear tetrahedral complex upon co-ordination of (R_P*,R_P*)-**58** to gold(I) and silver(I) is also to be investigated. The presence of three 1,2-phenylene linkages in the backbone of the ligand, and the fact that the two stereogenic phosphorus centres have the same relative configuration, should preclude formation of anything but a mononuclear tetrahedral gold(I) or silver(I) complex.

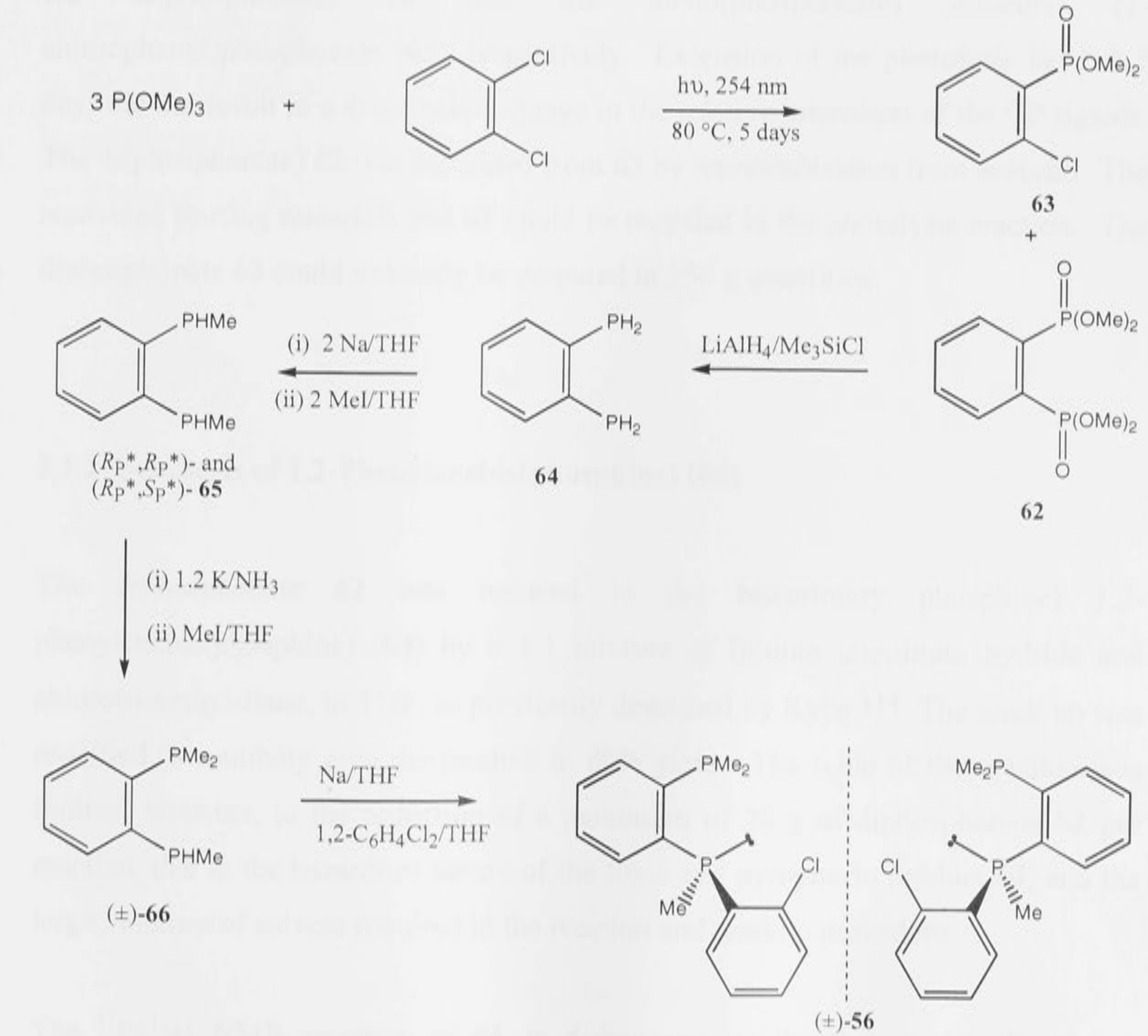
Chapter Two

Results and Discussion (I)

Synthesis and Resolution of (±)-(2-Chlorophenyl)(2-dimethylphosphinophenyl)methylphosphine

2.1 SYNTHESIS OF (±)-(2-CHLOROPHENYL)(2-DIMETHYL-PHOSPHINOPHENYL)METHYLPHOSPHINE [(±)-56]

The asymmetric di(tertiary phosphine) (±)-(2-chlorophenyl)(2-dimethylphosphino-phenyl)methylphosphine [(±)-**56**] was synthesised by the five-step synthesis outlined in Scheme 34.



Scheme 34

2.1.1 Synthesis of Tetramethyl 1,2-Phenylenebis(phosphonate) (62)

Photolysis of a 3:1 mixture of trimethyl phosphite and 1,2-dichlorobenzene at 80 °C, using a 400 W mercury vapour lamp, gave the diphosphonate tetramethyl 1,2-phenylenebis(phosphonate) (**62**) in 45% yield.[114] The optimal time for the reaction was found to be 5 days. The extent of the reaction could be monitored by $^{31}P\{^{1}H\}$ NMR spectroscopy, as the spectrum of the reaction mixture in d_1-chloroform typically contained three singlet resonances at δ 141.8, 19.2, and 18.3 for trimethyl phosphite, the di(phosphonate) **62** and the mono(phosphonate) dimethyl (2-chlorophenyl)phosphonate (**63**), respectively. Extension of the photolysis beyond 5 days did not result in a discernable change in the relative intensities of the ^{31}P signals. The di(phosphonate) **62** was separated from **63** by recrystallisation from acetone. The recovered starting materials and **63** could be recycled in the photolysis reaction. The diphosphonate **63** could routinely be prepared in 250 g quantities.

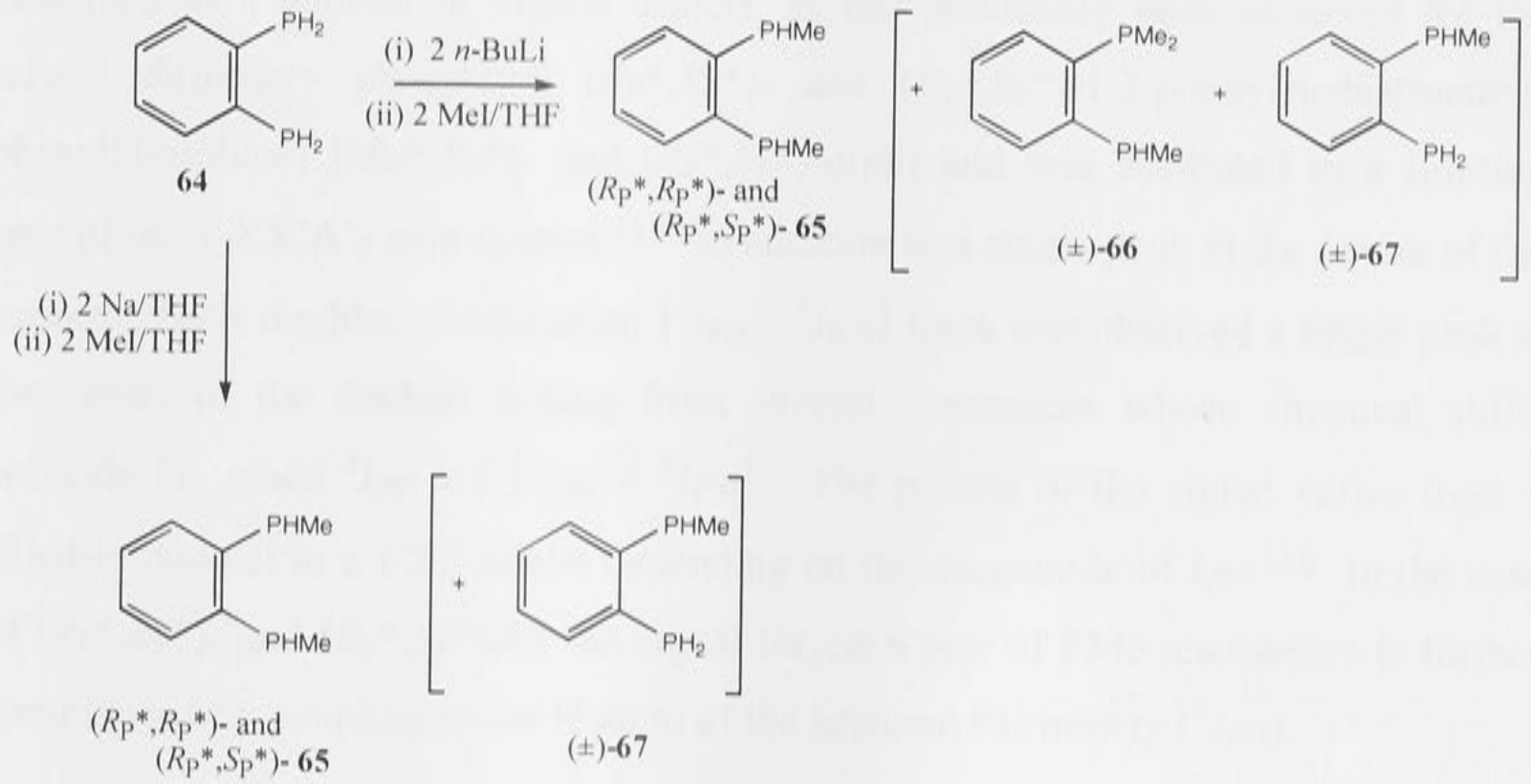
2.1.2 Synthesis of 1,2-Phenylenebis(phosphine) (64)

The diphosphonate **62** was reduced to the bis(primary phosphine) 1,2-phenylenebis(phosphine) (**64**) by a 1:1 mixture of lithium aluminum hydride and chlorotrimethylsilane, in THF, as previously described by Kyba.[114] The work up was modified to routinely give the product in 80% yield. The scale of the reaction was limited, however, to the reduction of a maximum of 20 g of diphosphonate **62** per reaction, due to the hazardous nature of the toxic and pyrophoric product **64**, and the large volumes of solvent required in the reaction and workup procedure.

The $^{31}P\{^{1}H\}$ NMR spectrum of **64**, in d_6-benzene, exhibited a singlet phosphorus resonance at δ -124.8, in agreement with the literature value. The ^{1}H NMR spectrum of **64** in the same solvent revealed a doublet of multiplet resonances for the PH_2 groups centred at δ 3.84 ($^{1}J_{PH}$ 207 Hz) and aromatic resonances from δ 6.82 - 7.24.

2.1.3 Synthesis of (R_P*,R_P*)- and (R_P*,S_P*)-1,2-Phenylenebis(methylphosphine) [(R_P*,R_P*)- and (R_P*,S_P*)-65]

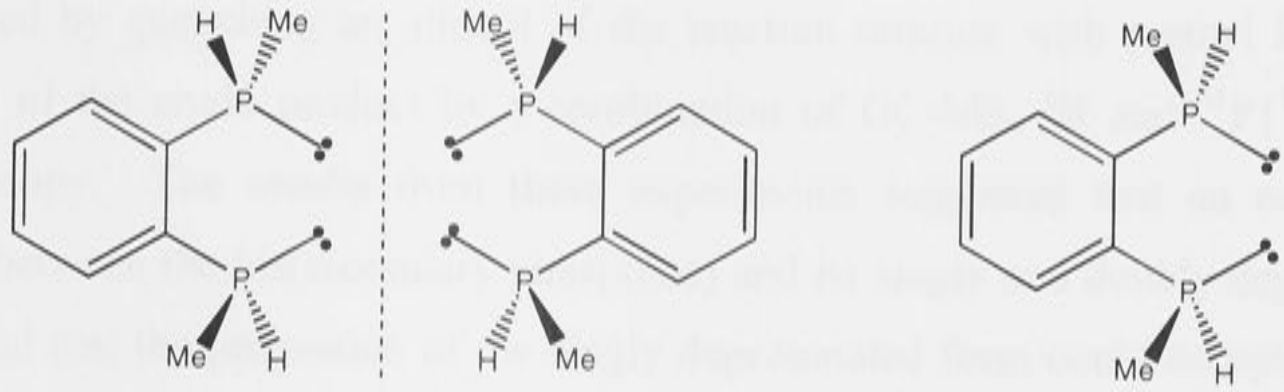
The bis(secondary phosphine) (R_P*,R_P*)- and (R_P*,S_P*)-1,2-phenylenebis(methylphosphine) [(R_P*,R_P*)- and (R_P*,S_P*)-**65**] was synthesised by double metalation of 1,2-phenylenebis(phosphine) (**64**) using either two equivalents of *n*-BuLi[114] or two equivalents of sodium in THF, followed by reaction with methyl iodide in THF (Scheme 35). The former approach gave a product that, after distillation, typically contained between 5-20% of (±)-(2-dimethylphosphinophenyl)methylphosphine [(±)-**66**] as well as small amounts of (±)-(2-methylphosphinophenyl)phosphine [(±)-**67**]. In the case of sodium, the reaction proved much cleaner and *ca* 5% of (±)-**67** was invariably present in the distilled product. These side products could not be removed by fractional distillation and the product was used without further purification.



Scheme 35

The $^{31}P\{^1H\}$ NMR spectrum of the bis(secondary phosphine) (R_P*,R_P*)- and (R_P*,S_P*)-**65** in d_6-benzene exhibited two singlet resonances at δ -73.6 and -74.7, consistent with the presence of both diastereomers. A doublet at δ -126.3 was also observed for the PH_2 group of (±)-**67**, although the *P*HMe resonance for this compound was obscured by the resonances for (R_P*,R_P*)- and (R_P*,S_P*)-**65**. Doublet resonances at δ -54.4 and -72.5 were attributed to the secondary phosphine (±)-**66**. The ^1H NMR spectrum of (R_P*,R_P*)- and (R_P*,S_P*)-**65** in the same solvent exhibited

two sets of P*Me* resonances as overlapping multiplets centred at δ 1.13 and 1.16, and a pair of P*H* resonances at δ 4.32 and 4.48. None of the resonances, however, could be assigned to one specific diastereomer. The two diastereomeric forms of the bis(secondary phosphine) are shown in Figure 8.



(R_P*,R_P*)-**65** (R_P*,S_P*)-**65**

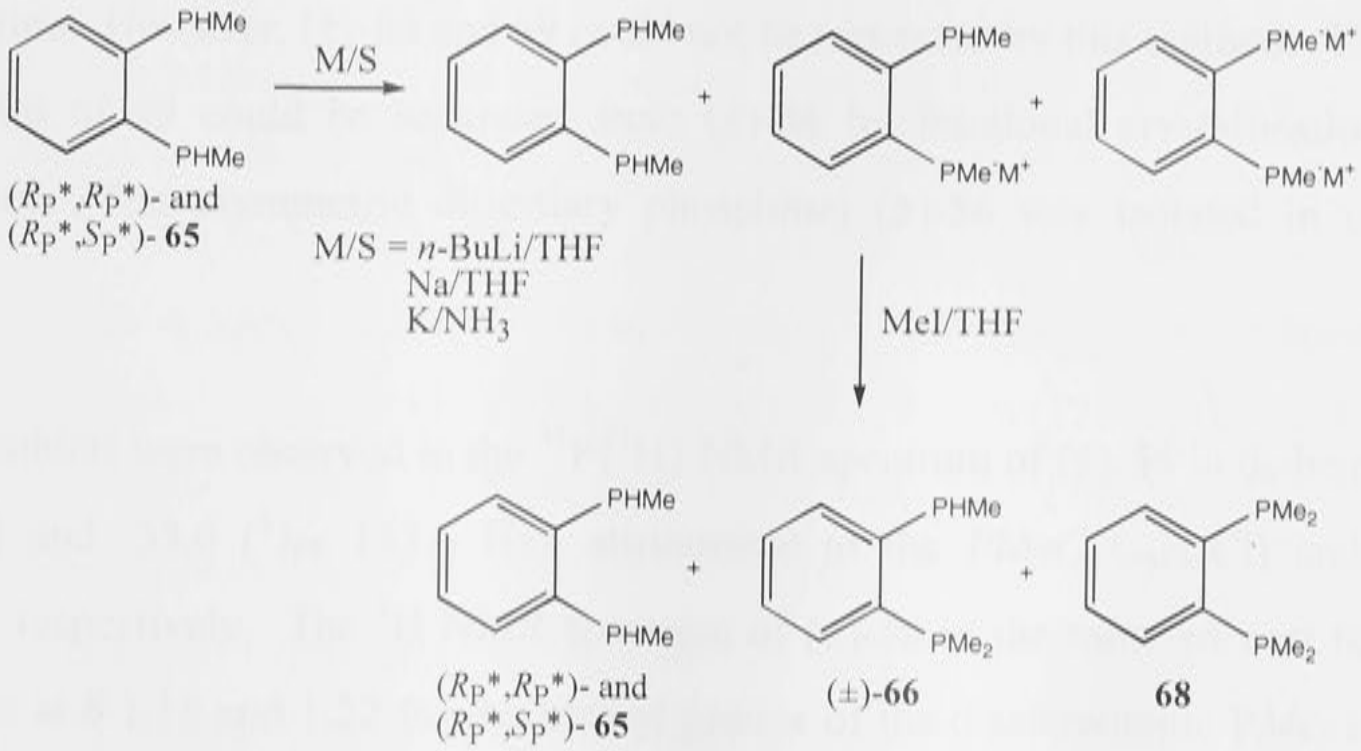
Figure 8 Diastereomerism in **65**.

The multiplets for the methyl resonances of (R_P*,R_P*)- and (R_P*,S_P*)-**65** can best be described as a doublet of virtual triplets, as has previously been observed for the related di(tertiary phosphine) (R_P*,R_P*)- and (R_P*,S_P*)-1,2-phenylenebis(methylphenylphosphine) [(R_P*,R_P*)- and (R_P*,S_P*)-diph] and was attributed to a limiting case of an $A_3XX'A'_3$ spin system.[115] In addition to a single peak at the centre of the expected basic doublet of separation $|^2J_{PH} + {}^5J_{P'H}|$ there was observed a single peak at the centre of the doublet arising from several resonances whose chemical shifts coincide i.e. when ${}^3J_{PP'} >> |^2J_{PH} + {}^5J_{P'H}|$. The pattern of the signal varies from a filled-in doublet to a 1:2:1 triplet depending on the magnitude of $J_{PP'}$.[116] In the case of (R_P*,R_P*)- and (R_P*,S_P*)-**65** the signal for each pair of PMe resonances is further complicated by coupling to the H atom of the adjacent PH moiety (${}^3J_{HH}$).

2.1.4 Synthesis of (±)-(2-Dimethylphosphinophenyl)methylphosphine [(±)-66]

Conversion of the bis(secondary phosphine) (R_P*,R_P*)- and (R_P*,S_P*)-**65** to the secondary phosphine (±)-(2-dimethylphosphinophenyl)methylphosphine [(±)-**66**] was achieved by mono-deprotonation of the bis(secondary phosphine) with *n*-BuLi in THF, sodium in THF, or with potassium in liquid ammonia. A mixture of three products was formed upon quenching the reaction mixture with methyl iodide:

unreacted bis(secondary phosphine) (R_P*,R_P*)- and (R_P*,S_P*)-**65**, secondary phosphine (±)-**66** and di(tertiary phosphine) 1,2-phenylenebis(dimethylphosphine) (**68**) (Scheme 36), indicating that the deprotonation of (R_P*,R_P*)- and (R_P*,S_P*)-**65** was not completely selective. In each case varying quantities of the metallating agent were added to the bis(secondary phosphine) and the progress of the reaction was monitored by quenching an aliquot of the reaction mixture with methyl iodide and analysis of the crude product by a combination of GC-MS, ^{1}H and ^{31}P{^{1}H} NMR spectroscopy. The results from these experiments suggested that an equilibrium existed between the bis(secondary phosphine) and its singly and doubly deprotonated forms and that the proportion of the singly deprotonated form could be optimised by the use of 1.2 equivalents of potassium in liquid ammonia. Under these conditions only small amounts (typically 5-10%) of unreacted bis(secondary phosphine) (R_P*,R_P*)- and (R_P*,S_P*)-**65** was present after the solution was quenched with methyl iodide. A significant amount (typically 20-25%) of di(tertiary phosphine) **68**, however, was present in the isolated product. These compounds could not be separated by fractional distillation and the mixture was used without further purification.



Scheme 36

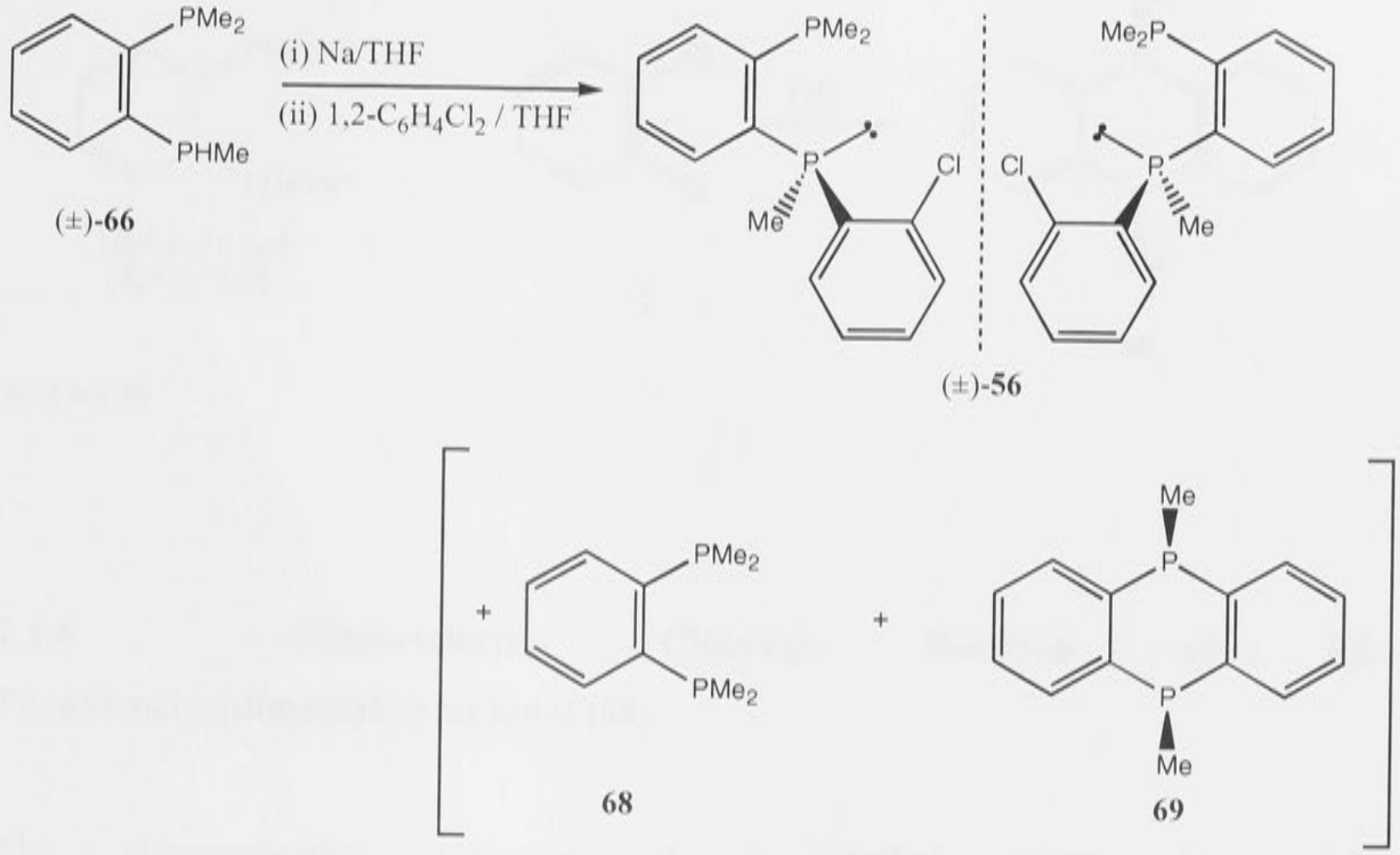
The ^{31}P{^{1}H} NMR spectrum of the *ca* 4:1 mixture of (±)-**66** and **68** in d_6-benzene exhibited two doublets at δ -54.4 and -72.5 ($^3J_{PP}$ 122.7 Hz) attributable to the *P*Me$_2$ and the *P*HMe groups of the secondary phosphine, respectively. A singlet ^{31}P resonance was observed for **68** at δ -54.8. The spectrum also contained minor

resonances for (R_P*,R_P*)- and (R_P*,S_P*)-**65** at δ -73.6 and -74.7. The ^{1}H NMR spectrum of the *ca* 4:1 mixture of (±)-**66** and **68** in the same solvent exhibited doublet resonances at δ 1.08 and 1.13, arising from the diastereotopic methyl groups of the P*Me*$_2$ moiety of (±)-**66**. A doublet of doublet of doublets at δ 1.27 and a doublet of doublet of quartets at δ 4.45 was observed for the PH*Me* and P*H*Me resonances of (±)-**66**, respectively. A multiplet was observed at δ 1.22 for the P*Me*$_2$ group of **68**.

2.1.5 Synthesis of (±)-(2-Chlorophenyl)(2-dimethylphosphinophenyl)-methylphosphine [(±)-56]

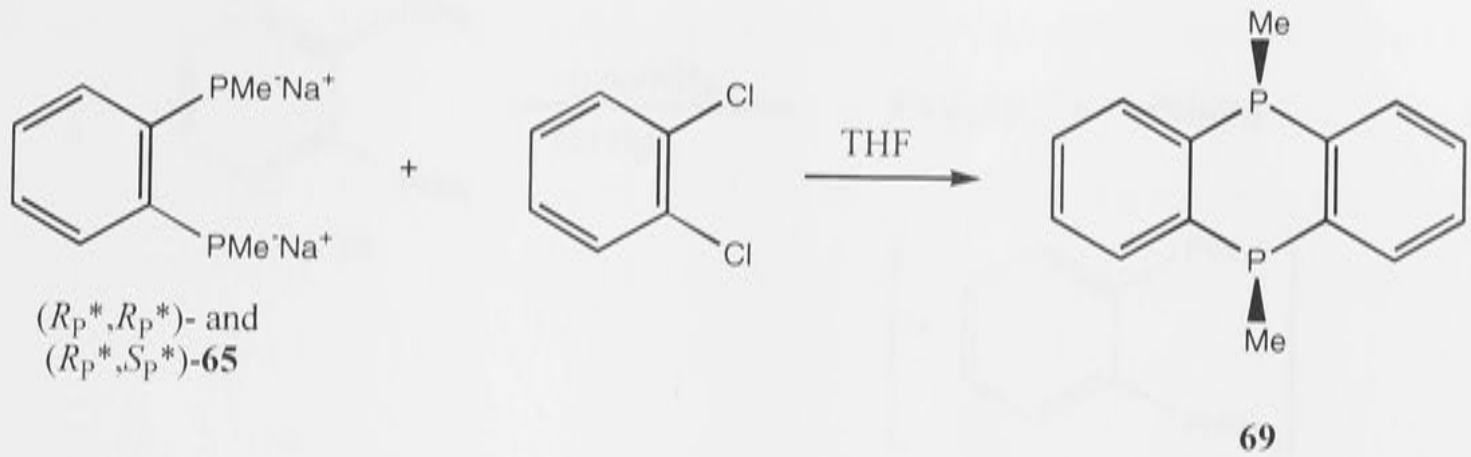
Reaction of the *ca* 4:1 mixture of (±)-**66** and **68** with sodium in THF, followed by reaction with 1,2-dichlorobenzene in THF, gave the asymmetric di(tertiary phosphine) (±)-(2-chlorophenyl)(2-dimethylphosphinophenyl)methylphosphine [(±)-**56**]. The crude product was a mixture of (±)-**56**, unreacted di(tertiary phosphine) **68** and small quantities of the heterocyclic compound 5-10-dimethyl-5,10-dihydrophosphanthren (**69**) (Scheme 37). Unreacted **68** was recovered from the crude product by fractional distillation. However, (±)-**56** and **69** could not be separated by this method. The trace quantities of **69** could be separated from (±)-**56** by fractional crystallisation from methanol. The asymmetric di(tertiary phosphine) (±)-**56** was isolated in *ca* 65% yield.

Two doublets were observed in the ^{31}P{^{1}H} NMR spectrum of (±)-**56** in d_6-benzene at δ -36.4 and -53.6 ($^3J_{PP}$ 153.6 Hz), attributable to the *P*Me(2-C_6H_4Cl) and *P*Me$_2$ groups, respectively. The ^{1}H NMR spectrum of (±)-**56** in the same solvent revealed doublets at δ 1.15 and 1.22 for the methyl groups of the diastereotopic P*Me*$_2$ moiety, and a similar resonance at δ 1.46 for the P*Me*(C_6H_4Cl-2) group. The mass spectrum of (±)-**56** gave the M^+ peak at m/e 294, as well as peaks at 279 $(M\text{-}Me)^+$ and 259 $(M\text{-}Cl)^+$, consistent with the presence of the di(tertiary phosphine).



Scheme 37

The $^{31}P\{^{1}H\}$ NMR spectrum of the heterocycle **69** in d_1-chloroform revealed a singlet at δ -38.2. The ^{1}H NMR spectrum in the same solvent exhibited a peak at δ 1.92 for the P*Me* group. The mass spectrum of the heterocycle gave a M^+ peak at m/e 244, a $(M\text{-}Me)^+$ peak at m/e 229, and a $(M\text{-}PMe)^+$ peak at 183. The heterocycle was presumably formed by the coupling of doubly deprotonated (R_P*,R_P*)- and (R_P*,S_P*)-**65** with 1,2-dichlorobenzene (Scheme 38). The presence of a single peak in the $^{31}P\{^{1}H\}$ NMR spectrum indicates that only one of the two possible diastereomers of **69** was generated. This finding is consistent with the work of Kyba *et al.*, who reacted the related lithium phosphide [lithium 1,2-phenylenebis(phenylphosphide)] with 1,2-phenylenebis[(3-chloropropyl)phenylphosphine] to stereoselectively generate macrocyclic ligands where the phenyl groups off adjacent phosphorus atoms connected by 1,2-phenylene linkages had the same disposition (section 1.3.2, Scheme 5).[54]



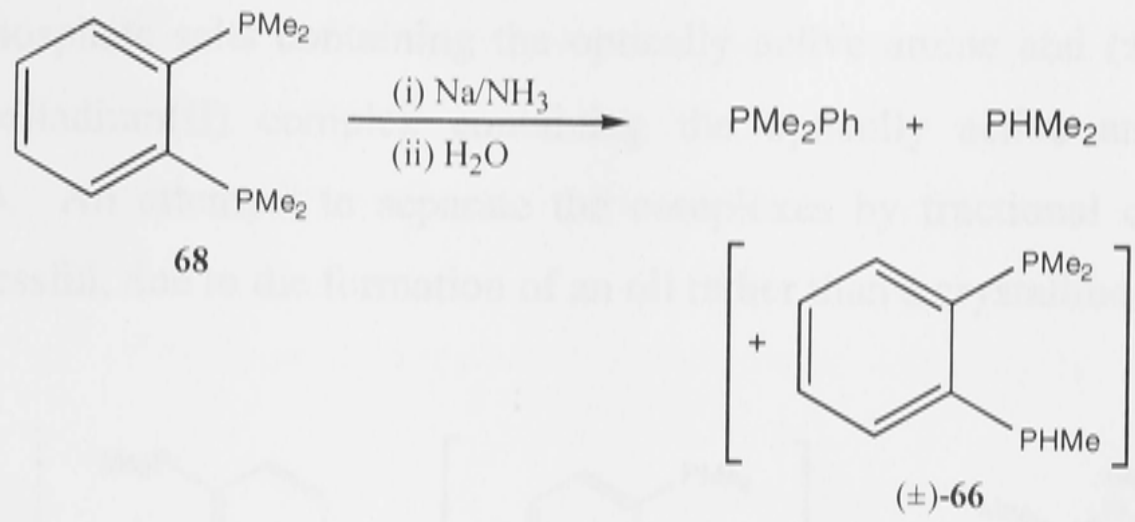
(R_P*,R_P*)- and
(R_P*,S_P*)-**65**

69

Scheme 38

2.1.6 Chemoselective Cleavage Reaction of 1,2-Phenylenebis(dimethylphosphine) (68)

The chemoselective cleavage of a methyl group from 1,2-phenylenebis(dimethylphosphine) (**68**) by sodium in liquid ammonia was investigated as a possible alternative route to the secondary phosphine (±)-**66**. Carlton and Cook have previously reported the analogous reaction for the chemoselective cleavage of a methyl group from the di(tertiary arsine) analogue 1,2-phenylenebis(dimethylarsine) to give the secondary arsine (±)-(2-dimethylarsinophenyl)methylarsine.[117] Little evidence for the chemoselective cleavage of a methyl group from **68**, however, was observed under these reaction conditions. The crude product from the hydrolysed reaction mixture of **68** and sodium in liquid ammonia was analysed by GC-MS and was found to contain dimethylphenylphosphine as the primary product, and trace quantities of the secondary phosphine (±)-**66** (*ca* 3%). This was consistent with cleavage of a single dimethylphosphino group from **68** to give dimethylphenylphosphine and dimethylphosphine (Scheme 39). Dimethylphosphine was presumably removed along with the solvent during the work-up procedure. The chemoselective cleavage of aryl groups from tertiary phosphines by alkali metals is well known.[97,112,118]



68

(±)-**66**

Scheme 39

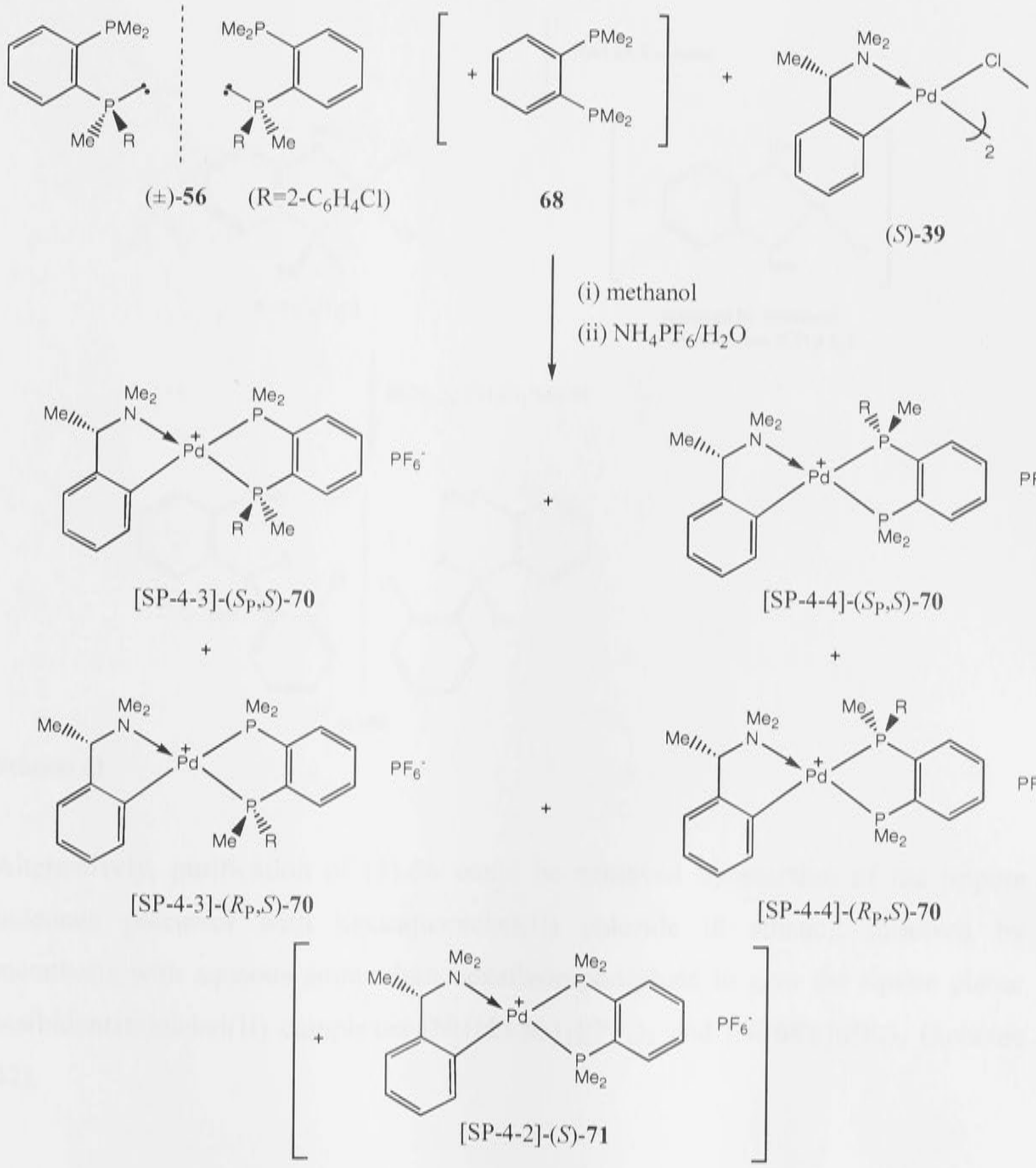
2.2 RESOLUTION OF (±)-(2-CHLOROPHENYL)(2-DIMETHYL-PHOSPHINOPHENYL)METHYLPHOSPHINE, (±)-56

2.2.1 Separation of (±)-56 from Trace Quantities of 68

The resolution of (±)-(2-chlorophenyl)(2-dimethylphosphinophenyl)methylphosphine [(±)-**56**] by the method of metal complexation was investigated during the course of this work. The procedure involves a bridge splitting reaction between the racemic ligand and a chloro-bridged palladium(II) dimer containing an ortho-metalated optically active amine, *viz.* (*R*)-dimethyl(1-phenylethyl)amine, (*R*)-dimethyl[1-(1-naphthyl)ethyl]amine, or their enantiomers, in methanol. The resulting pair of internally diastereomeric palladium(II) complexes are invariably isolated as hexafluorophosphate salts which are separable by fractional crystallisation from a suitable solvent system. This method has previously been used to resolve a range of bidentate ligands containing stereogenic tertiary phosphorus (or arsenic) donor atoms.[119]

Initial attempts to resolve (±)-**56** by this method, however, were thwarted by the presence of small quantities of the di(tertiary phosphine) **68**. For example, reaction of (±)-**56** with di-μ-chloro-bis{(*S*)-2-[(1-dimethylamino)ethyl]phenylC^1,N}-dipalladium(II) [(*S*)-**39**] in methanol, followed by the addition of aqueous ammonium hexafluorophosphate, gave an inseparable mixture of four diastereomeric

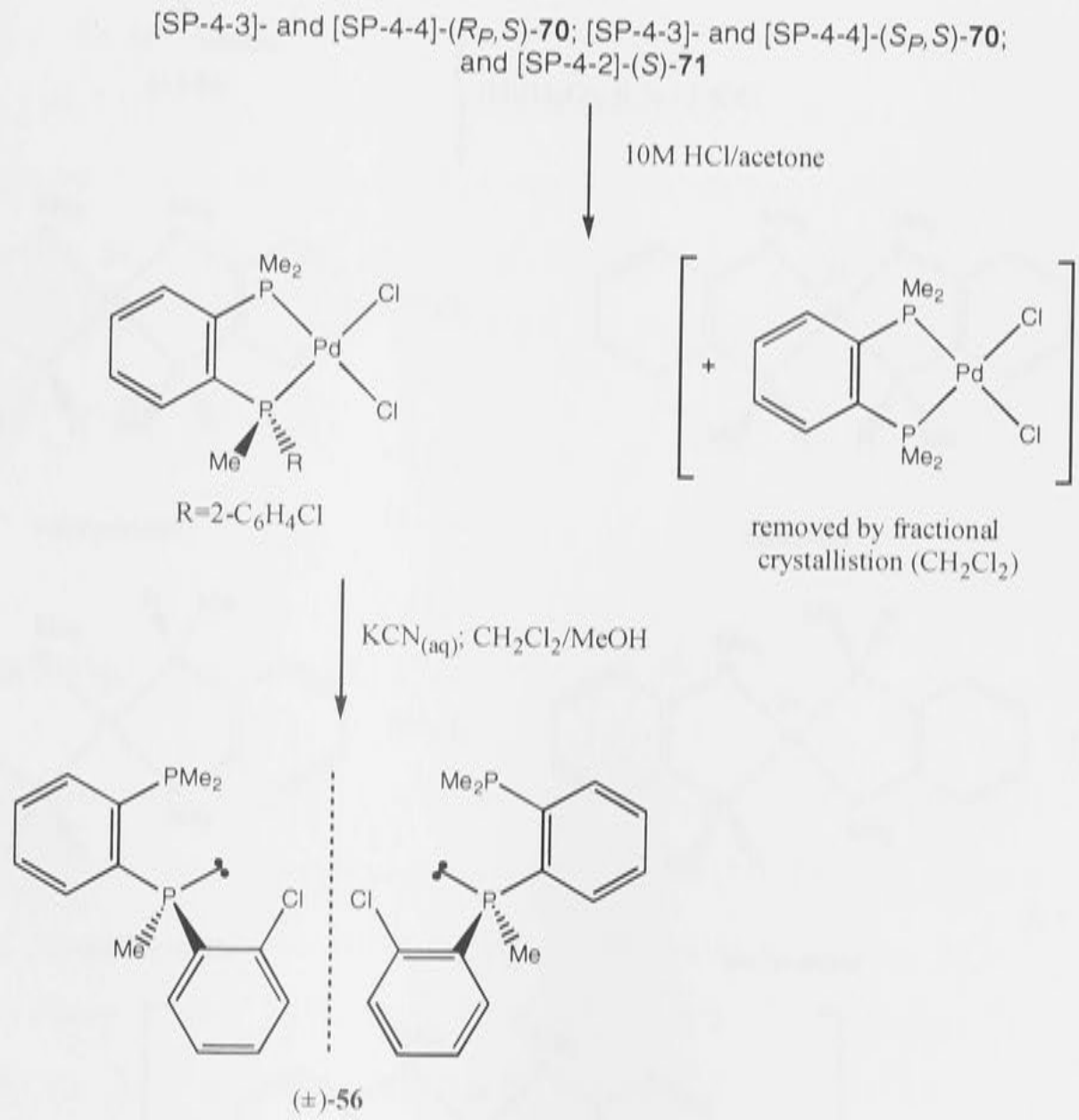
hexafluorophosphate salts containing the optically active amine and (±)-**56**, and an analogous palladium(II) complex containing the optically active amine and **68** (Scheme 40). All attempts to separate the complexes by fractional crystallisation were unsuccessful, due to the formation of an oil rather than a crystalline product.



Scheme 40

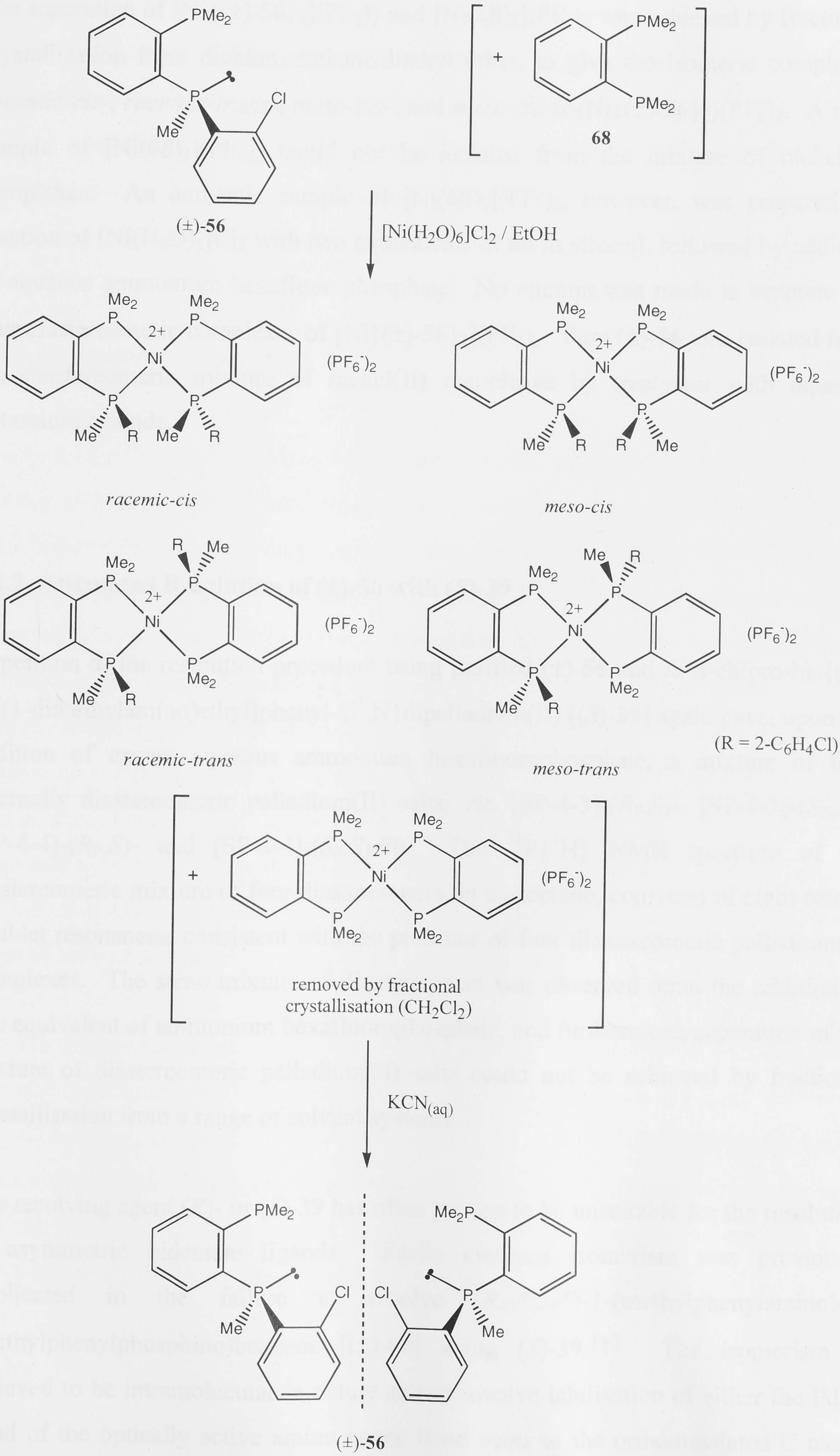
The mixture of hexafluorophosphate salts **70** and **71** were converted to the corresponding dichloropalladium(II) complexes (±)-[$PdCl_2${(±)-**56**}] and [$PdCl_2$(**68**)] by treatment with concentrated hydrochloric acid in acetone. Separation of the

dichloropalladium(II) complexes was achieved by fractional crystallisation from dichloromethane. Pure (±)-**56** was obtained upon treatment of (±)-[$PdCl_2${(±)-**56**}] with potassium cyanide in dichloromethane/methanol (Scheme 41).



Scheme 41

Alternatively, purification of (±)-**56** could be achieved by reaction of the impure bidentate precursor with hexaaquanickel(II) chloride in ethanol, followed by metathesis with aqueous ammonium hexafluorophosphate to give the square planar bis(bidentate)nickel(II) complexes [Ni{(±)-**56**}$_2$]$(PF_6)_2$ and [Ni(**68**)$_2$]$(PF_6)_2$ (Scheme 42).


PMe2
Cl
Me
(±)-56
+
PMe2
PMe2
68
[Ni(H2O)6]Cl2 / EtOH
Me2
P
2+
Ni
(PF6-)2
R
racemic-cis
meso-cis
racemic-trans
meso-trans
removed by fractional crystallisation (CH2Cl2)
KCN(aq)
(R = 2-C6H4Cl)

Scheme 42

The separation of [Ni{(±)-**56**}$_2$](PF$_6$)$_2$ and [Ni(**68**)$_2$](PF$_6$)$_2$ was achieved by fractional crystallisation from dichloromethane/diethyl ether, to give the isomeric complexes *racemic-cis*-, *racemic-trans*-, *meso-cis*-, and *meso-trans*-[Ni{(±)-**56**}$_2$](PF$_6$)$_2$. A pure sample of [Ni(**68**)$_2$](PF$_6$)$_2$ could not be isolated from the mixture of nickel(II) complexes. An authentic sample of [Ni(**68**)$_2$](PF$_6$)$_2$, however, was prepared by reaction of [Ni(H$_2$O)$_6$]Cl$_2$ with two equivalents of **68** in ethanol, followed by addition of aqueous ammonium hexafluorophosphate. No attempt was made to separate the four diastereomeric complexes of [Ni{(±)-**56**}$_2$](PF$_6$)$_2$. Pure (±)-**56** was isolated from the diastereomeric mixture of nickel(II) complexes by treatment with aqueous potassium cyanide.

2.2.2 Attempted Resolution of (±)-56 with (*S*)-39

Repetition of the resolution procedure using purified (±)-**56** and di-μ-chloro-bis{(*S*)-2-[(1-dimethylamino)ethyl]phenyl-C^1,N}dipalladium(II) [(*S*)-**39**] again gave, upon the addition of excess aqueous ammonium hexafluorophosphate, a mixture of four internally diastereomeric palladium(II) salts; *viz*. [SP-4-3]-(R_P,*S*)-, [SP-4-3]-(S_P,*S*)-, [SP-4-4]-(R_P,*S*)- and [SP-4-4]-(S_P,*S*)-**70**. The ^{31}P{^{1}H} NMR spectrum of the diastereomeric mixture of four diastereomers, in d$_6$-acetone, consisted of eight sets of doublet resonances, consistent with the presence of four diastereomeric palladium(II) complexes. The same mixture of diastereomers was observed upon the addition of one equivalent of ammonium hexafluorophosphate, and furthermore, separation of the mixture of diastereomeric palladium(II) salts could not be achieved by fractional crystallisation from a range of solvent systems.

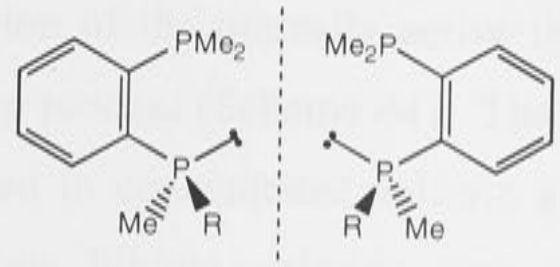
The resolving agent (*R*)- or (*S*)-**39** has often proven to be unsuitable for the resolution of asymmetric bidentate ligands. Facile cis/trans isomerism was previously implicated in the failure to resolve (R_{As}*,S_P*)-1-(methylphenylarsino)-2-(methylphenylphosphino)benzene [(±)-**60**] using (*S*)-**39**.[112] The isomerism is believed to be intramolecular in nature and to involve labilisation of either the Pd-N bond of the optically active amine or the bond *trans* to the orthometalated C atom. Diastereoisomerism arising from λ/δ conformations of the chelate ring containing the

orthometalated C atom was also observed in the unsuccessful attempted resolution of (±)-[1-(2-diphenylphosphino-1-naphthyl)isoquinoline [(±)-quinap] using (S)-**39**. Both of these ligands, however, were successfully resolved using the analogous chloro-bridged palladium(II) dimer di-μ-chlorobis{(*S*)-[1-(dimethylamino)ethyl]naphthyl-C^2,N}dipalladium(II) [(*S*)-**72**], or its enantiomer.[120,121]

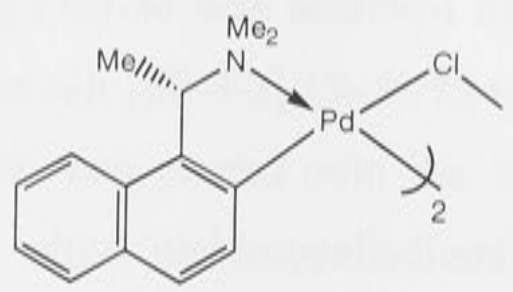
2.2.3 Resolution of (±)-56 with (*S*)-72

Reaction of (±)-**56** with the resolving agent [(*S*)-**72**] in methanol, followed by the addition of excess aqueous ammonium hexafluorophosphate, again gave a mixture of four diastereomeric hexafluorophosphate salts; *viz*. [SP-4-3]-(R_P,*S*)-, [SP-4-3]-(S_P,*S*)-, [SP-4-4]-(R_P,*S*)- and [SP-4-4]-(S_P,*S*)-**73** (Scheme 43). The same mixture of four diastereomeric palladium(II) salts was observed on addition of only one equivalent of aqueous ammonium hexafluorophosphate. Fractional crystallisation of the diastereomeric mixture from chloroform/propan-2-ol resulted in the isolation of a 1:1 mixture of [SP-4-3]-(R_P,*S*)- and [SP-4-3]-(S_P,*S*)-**73**, $[\alpha]_D$ = +93 ° (dichloromethane). The mother liquor from the isolation of [SP-4-3]-(R_P,*S*)- and [SP-4-3]-(S_P,*S*)-**73** contained a *ca* 1:1:9:9 mixture of [SP-4-3]-(R_P,*S*)-, [SP-4-3]-(S_P,*S*)-, [SP-4-4]-(R_P,*S*)- and [SP-4-4]-(S_P,*S*)-**73**, that could not be separated by fractional crystallisation from a range of solvent systems.

The 1:1 distereomeric mixture of [SP-4-3]-(R_P,*S*)- and [SP-4-3]-(S_P,*S*)-**73** was twice recrystallised from acetone/propan-2-ol to give diastereomerically pure [SP-4-3]-(S_P,*S*)-**73** as fine, colourless prisms of X-ray quality, $[\alpha]_D$ = +74 ° (dichloromethane). The mother liquor, which was enriched in [SP-4-3]-(R_P,*S*)-**73**, was taken to dryness and the residue was recrystallised from dichloromethane/propan-2-ol to give pure [SP-4-3]-(R_P,*S*)-**73**, $[\alpha]_D$ = +225 ° (dichloromethane) (Scheme 43).

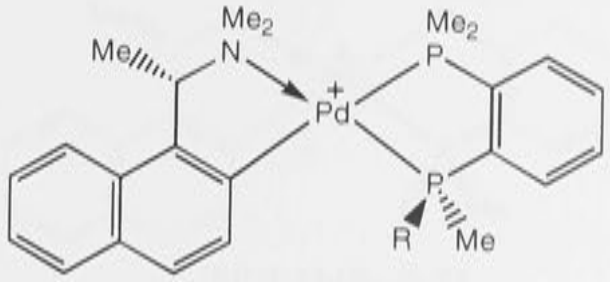


(±)-**56** (R=2-C_6H_4Cl)



(*S*)-**72**

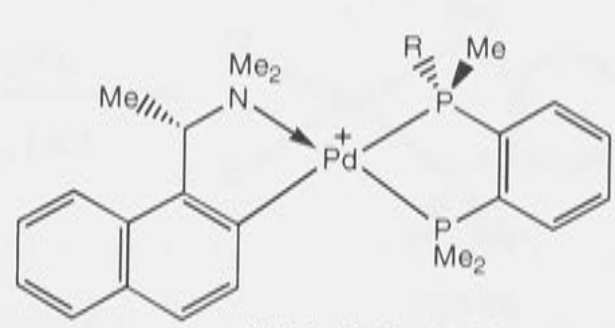
(i) methanol
(ii) NH_4PF_6/H_2O



PF_6^-

[SP-4-3]-(S_P,*S*)-**73**

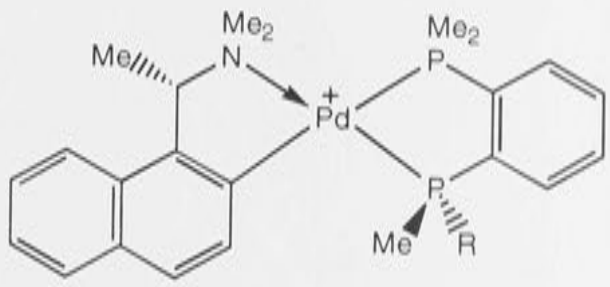
+



PF_6^-

[SP-4-4]-(S_P,*S*)-**73**

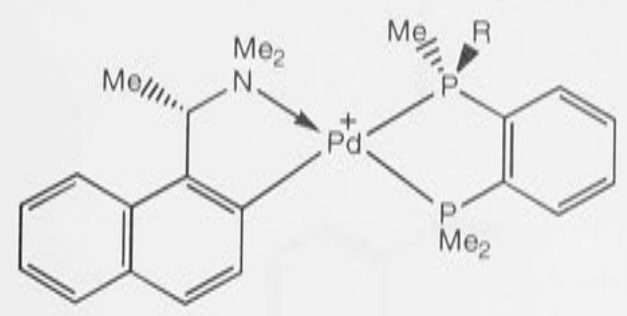
+



PF_6^-

[SP-4-3]-(R_P,*S*)-**73**

+



PF_6^-

[SP-4-4]-(R_P,*S*)-**73**

$CHCl_3$/propan-2-ol

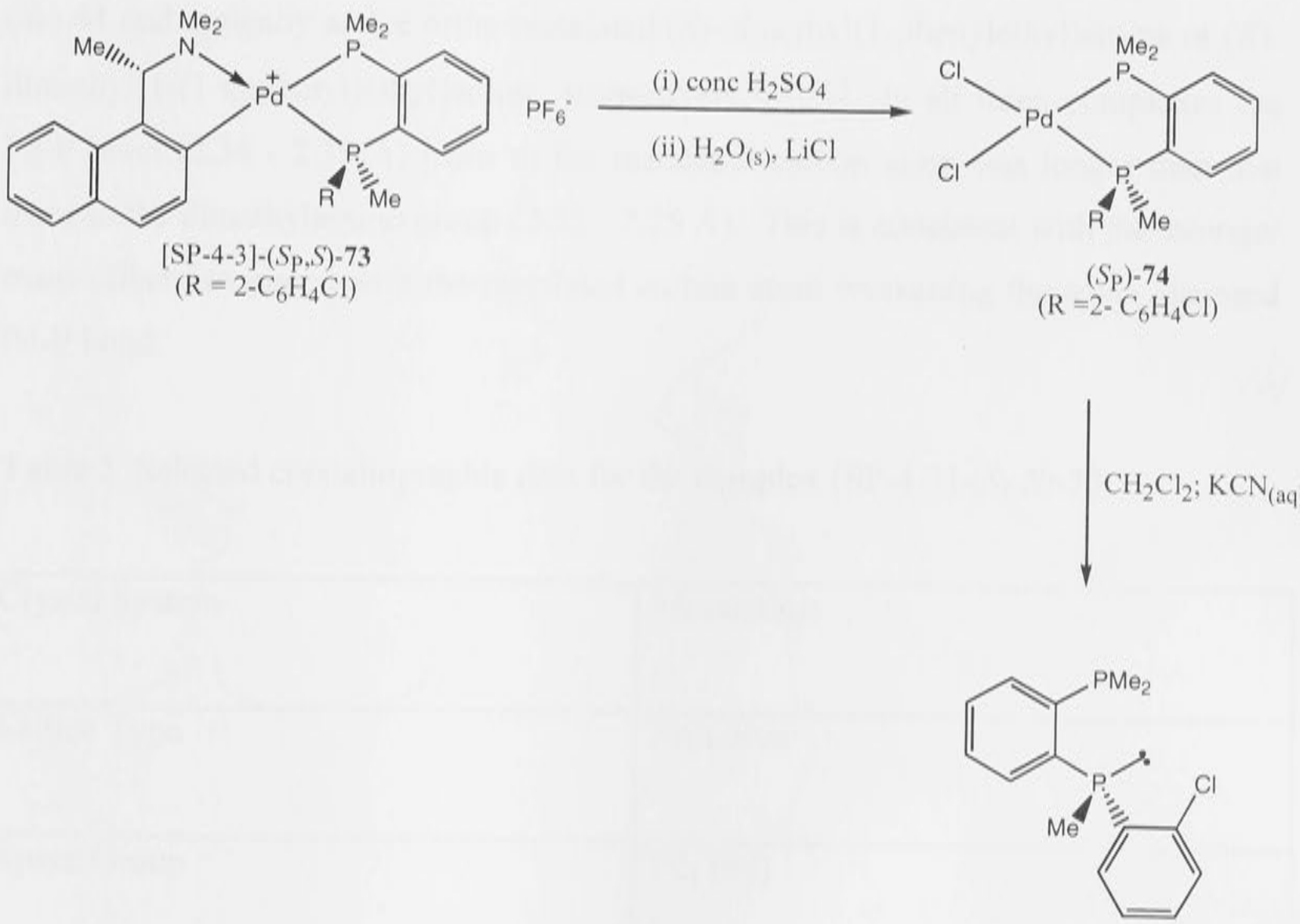
[SP-4-3]-(S_P,*S*)- and [SP-4-3]-(R_P,*S*)- **73**

acetone/propan-2-ol

[SP-4-3]-(S_P,*S*)-**73** ← Filter → CH_2Cl_2/propan-2-ol → [SP-4-3]-(R_P,*S*)-**73**

Scheme 43

Liberation of the optically active di(tertiary phosphine) (R_P)-**56** was achieved by a two-step process (Scheme 44). The hexafluorophosphate salt [SP-4-3]-(S_P,*S*)-**73** was dissolved in concentrated sulfuric acid, the solution was then poured onto ice, and anhydrous lithium chloride was added to give the white dichloropalladium(II) complex (S_P)-**74**, $[\alpha]_D$ = +52 ° (dichloromethane). Treatment of (S_P)-**74** with potassium cyanide gave the optically pure enantiomer (R_P)-**56**, $[\alpha]_D$ = +33 ° (dichloromethane).



[SP-4-3]-(S_P,*S*)-**73**
(R = 2-C_6H_4Cl)

(S_P)-**74**
(R =2- C_6H_4Cl)

(R_P)-**56**

Scheme 44

2.2.4 Crystal Structure Determination of the Complex [SP-4-3]-(S_P,*S*)-73

The absolute configuration of (R_P)-**56** was confirmed by a single crystal X-ray structure determination of the internally diastereomeric complex [SP-4-3]-(S_P,*S*)-**73**. Selected crystallographic data, bond lengths and angles are given in Tables 2 and 3.

The molecular structure of the cation of [SP-4-3]-(S_P,*S*)-**73** is shown in Figure 9. The structural data clearly shows that the phosphorus stereocentre of the di(tertiary phosphine) is coordinated *trans* to the NMe_2 group of the optically active naphthylamine and that the absolute configurations of the stereogenic phosphorus and carbon atoms are both *S*. The palladium(II) centre has a slightly distorted square planar geometry. The bond lengths and angles around the palladium(II) centre are in very close agreement to those associated with related diastereomerically pure palladium(II) complexes containing the asymmetric di(tertiary phosphines) (S_P)-**60** or (S_P)-**61** and optically active ortho-metalated (*S*)-dimethyl(1-phenylethyl)amine or (*R*)-dimethyl[1-(1-naphthyl)ethyl]amine, respectively.[112,113] In all three complexes the Pd-P bond (2.34 - 2.38 Å) *trans* to the metalated carbon atom was longer than that *trans* to the dimethylamino group (2.22 - 2.25 Å). This is consistent with the stronger *trans* effect associated with the metalated carbon atom weakening the *trans* disposed Pd-P bond.

Table 2 Selected crystallographic data for the complex [SP-4-3]-(S_P,*S*)-**73**.

Crystal System	Monoclinic
Lattice Type	Primitive
Space Group	$P2_1$ (#4)
Lattice Parameters	a = 8.982(2) Å b = 13.436(2) Å c = 13.797(2) Å β = 102.87(1)° V = 1623.2(5) $Å^3$

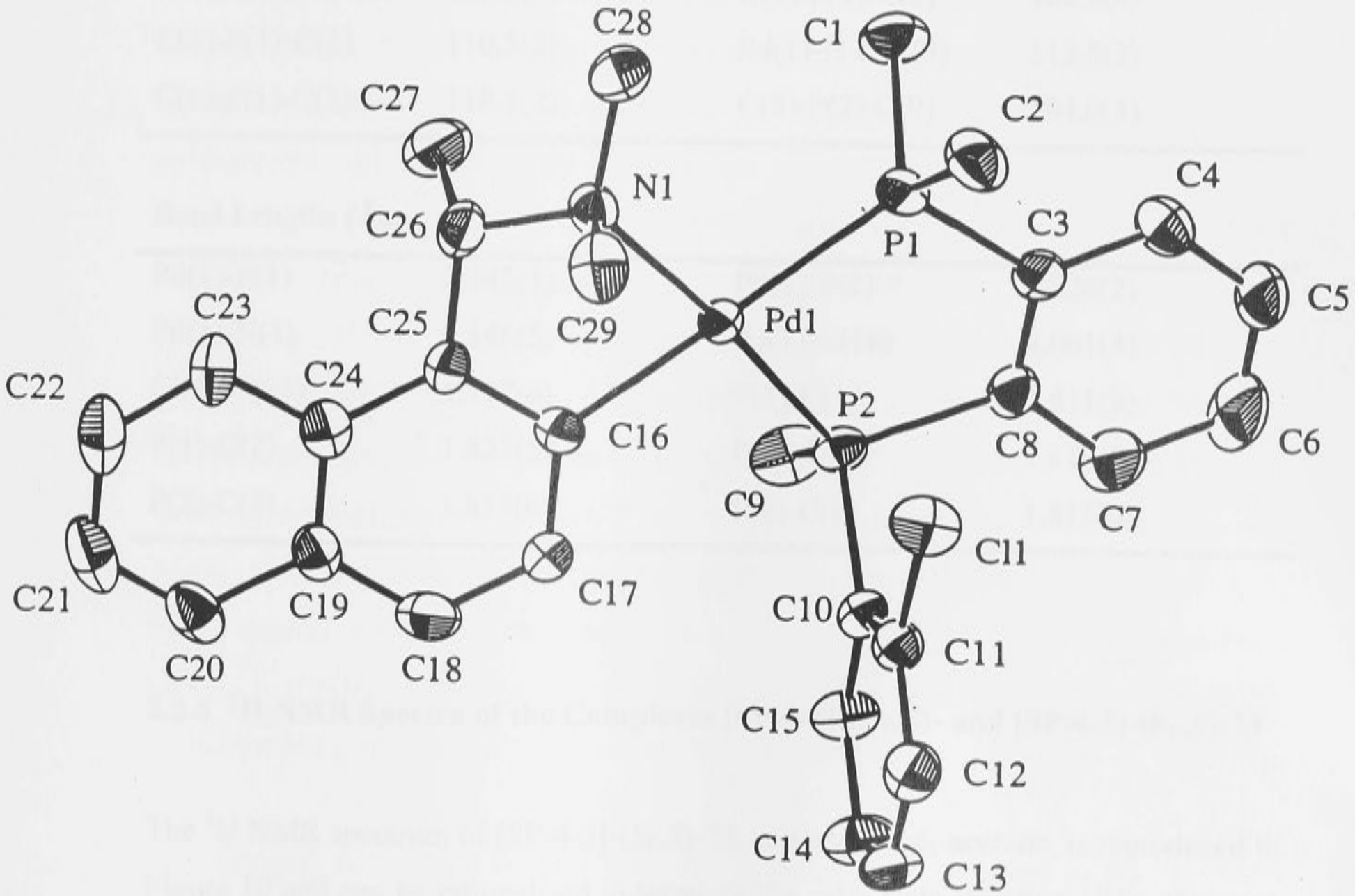


Figure 9 Molecular structure of the cation of [SP-4-3]-(S_P,S)-**73**.

Table 3 Selected bond angles and lengths for the complex [SP-4-3]-(S_P,*S*)-**73**.

Bond Angles (°).			
P(1)-Pd(1)-P(2)	85.36(7)	P(1)-Pd(1)-N(1)	99.5(1)
P(1)-Pd(1)-C(16)	177.5(2)	P(2)-Pd(1)-N(1)	175.1(1)
P(2)-Pd(1)-C(16)	94.4(2)	N(1)-Pd(1)-C(16)	80.8(3)
Pd(1)-P(1)-C(1)	117.9(3)	Pd(1)-P(1)-C(2)	117.5(2)
Pd(1)-P(1)-C(1)	107.9(3)	C(1)-P(1)-C(2)	105.3(4)
Pd(1)-P(1)-C(3)	103.6(3)	C(2)-P(1)-C(3)	102.8(4)
C(1)-P(1)-C(3)	110.5(2)	Pd(1)-P(2)-C(9)	112.8(2)
C(1)-P(1)-C(3)	119.3(2)	C(8)-P(2)-C(9)	104.0(3)
Bond Lengths (Å)			
Pd(1)-P(1)	2.343(1)	Pd(1)-P(2)	2.226(2)
Pd(1)-N(1)	2.146(5)	Pd(1)-C(16)	2.061(4)
Cl(1)-C(11)	1.737(6)	P(1)-C(1)	1.811(9)
P(1)-C(2)	1.823(5)	P(1)-C(3)	1.816(8)
P(2)-C(8)	1.835(6)	P(2)-C(9)	1.813(6)

2.2.5 ^{1}H NMR Spectra of the Complexes [SP-4-3]-(R_P,*S*)- and [SP-4-3]-(S_P,*S*)-73

The ^{1}H NMR spectrum of [SP-4-3]-(S_P,*S*)-**73**, recorded in d_6-acetone, is reproduced in Figure 10 and can be rationalised in terms of the solid state structure. The spectrum exhibited a doublet at δ 1.93 for the C*Me* group, a doublet for each diastereotopic methyl group of the PMe_2 moiety at δ 2.11 and 2.13, and a doublet at δ 2.36 for the methyl group of the stereogenic phosphorus centre. A singlet and broad multiplet, at δ 2.97 and 3.42, respectively, for the diastereotopic NMe_2 moiety, and a multiplet at δ 4.79 for the methine resonance, was also observed. The presence of a doublet of doublets at δ 6.85 for the γ-H of the ortho-metalated naphthyl moiety (i.e the H atom attached to C17 in Figure 9), well removed from the other aromatic resonances, provided evidence that the complex retained the same regio- and stereo-chemistry in

solution. The upfield shift (υ = 120 Hz) of this resonance is caused by shielding of the γ-H of the naphthyl moiety by the 2-chlorophenyl substituent of the adjacent stereogenic phosphorus atom.

A similar finding has previously been observed in the ^{1}H NMR spectra of related diastereomeric palladium(II) complexes containing the orthometalated optically active amine (*R*)- or (*S*)-dimethyl[1-(1-(naphthyl)ethyl]amine and a range of optically active bidentate ligands containing at least one phosphorus (or arsenic) stereocentre bearing a methyl and an aryl substituent. In all of these cases, including [SP-4-3]-(S_P,*S*)-**73**, an upfield shift of γ-H was only observed when the methyl groups of the stereogenic carbon atom and the *trans* disposed phosphorus (or arsenic) stereocentre were in a *syn* arrangement with respect to the coordination plane of the palladium(II) centre. The observation of an upfield shift of the γ-H resonance clearly provides a means of assigning absolute configurations to complexes of this type by ^{1}H NMR spectroscopy.[119] It should be noted that the magnitude of the upfield shift of γ-H is much smaller, and therefore the method of assignment is much less reliable, when the moiety containing the two donor atoms is a 1,2-ethylene moiety[113] rather than the more rigid 1,2-phenylene group.[122] The γ-H resonance in these complexes was also found to be coupled to the adjacent stereogenic phosphorus atom in the respective ^{1}H NMR spectra, *via* what is believed to be a through-space rather than a through-bond effect. A similar effect was apparent in the ^{1}H NMR spectrum of [SP-4-3]-(S_P,*S*)-**73**, a $^4J_{PH}$ coupling constant of 14 Hz being observed for γ-H.

Accordingly, no upfield shift of the γ-H resonance was observed in the ^{1}H NMR spectrum of [SP-4-3]-(R_P,*S*)-**73** (Figure 11). The ^{1}H NMR spectrum of [SP-4-3]-(R_P,*S*)-**73** in d_6-acetone was also consistent with the presence of a single diastereomeric complex, and revealed a doublet at δ 1.87 for the C*Me* group, two superimposed doublets at δ 2.13 for the diastereotopic methyl resonances of the P*Me*$_2$ moiety, a doublet at δ 2.57 for the P*Me* group, a singlet and a multiplet resonance at δ 2.97 and 3.41, respectively, for the N*Me*$_2$ groups, and a multiplet at δ 4.78 for the methine resonance. Selected ^{1}H NMR data for [SP-4-3]-(R_P,*S*)- and [SP-4-3]-(S_P,*S*)-**73** are given in Table 4.

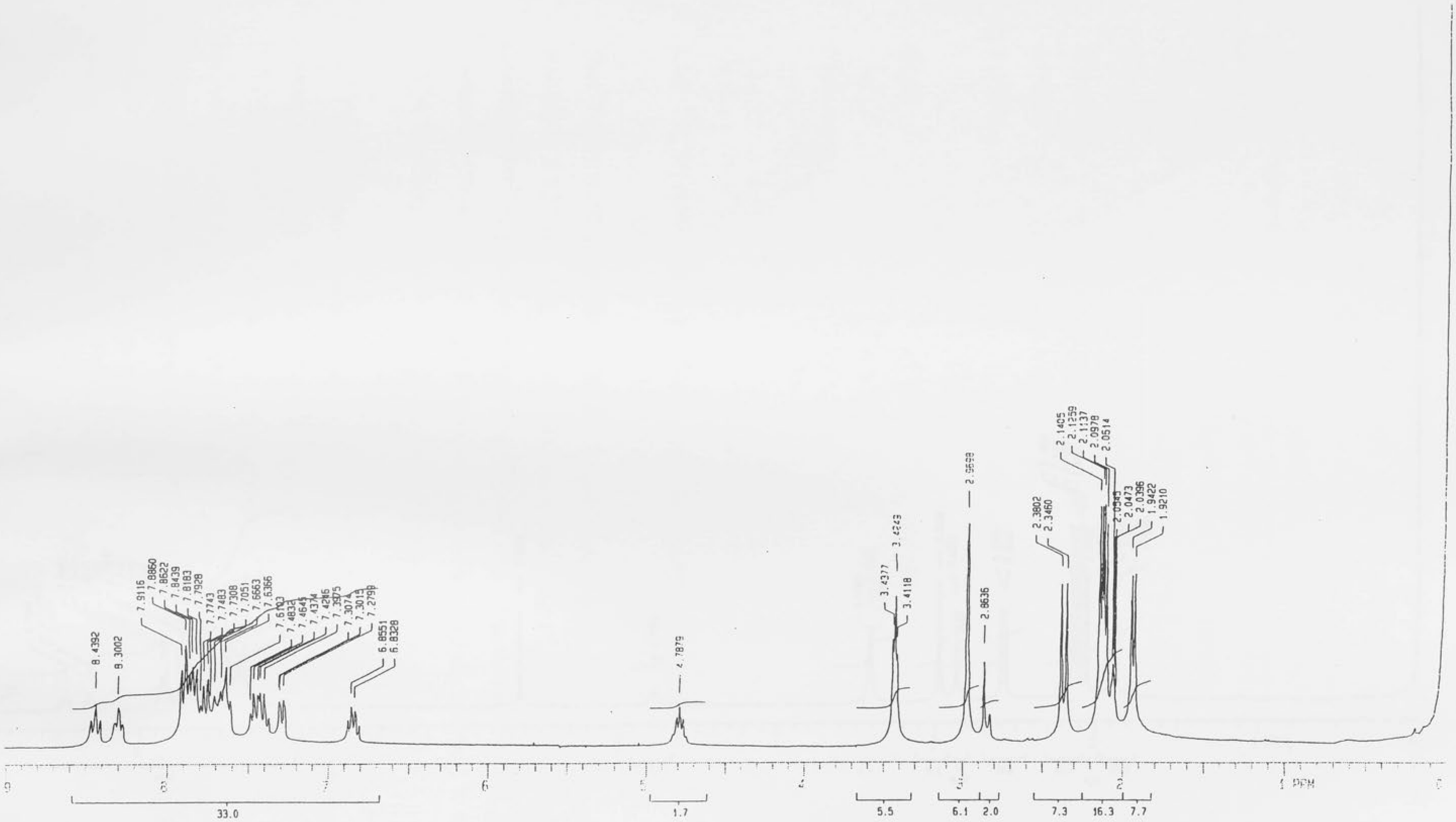


Figure 10 ^{1}H NMR spectra of [SP-4-3-(S_P,S)]-**73** in d_6-acetone.

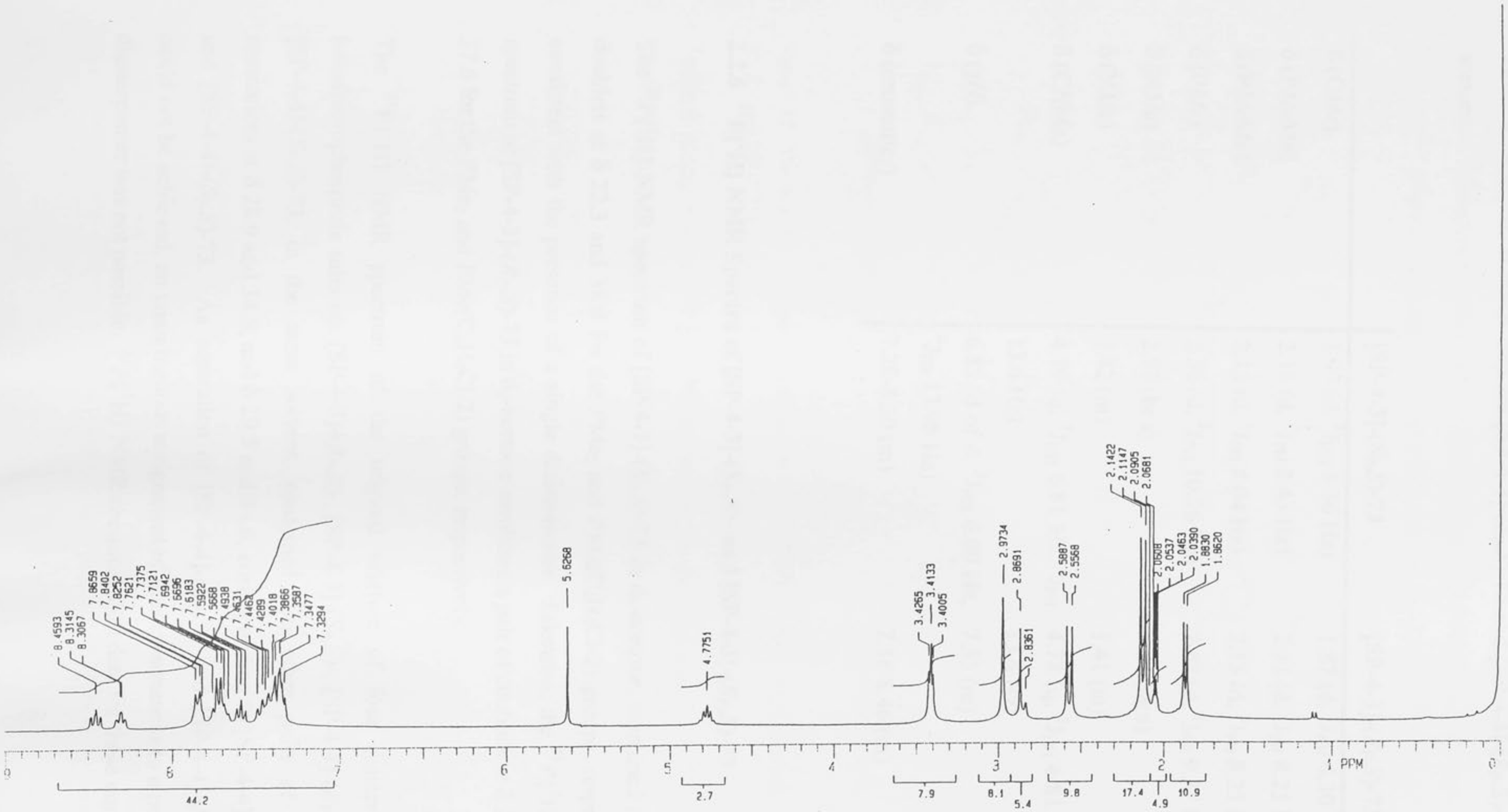


Figure 11 ^{1}H NMR spectra of [SP-4-3-(R_P,S)]-**73** in d_6-acetone.

Table 4 Selected ^{1}H NMR data for [SP-4-3]-(S_P,*S*)-**73** and [SP-4-3]-(R_P,*S*)-**73** in d_6-acetone.

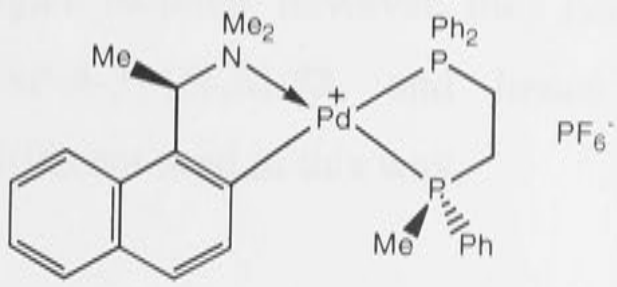
	[SP-4-3]-(S_P,*S*)-**73**	[SP-4-3]-(R_P,*S*)-**73**
δ (C*Me*)	1.93 (d, $^{3}J_{HH}$ 6.36 Hz)	1.87 (d, $^{3}J_{HH}$ 6.30 Hz)
δ (P*Me*Me)	2.11 (d, $^{2}J_{PH}$ 8.43 Hz)	2.13 (d, $^{2}J_{PH}$ 8.25 Hz)
δ (P*Me*Me)	2.13 (d, $^{2}J_{PH}$ 8.04 Hz)	2.13 (d, $^{2}J_{PH}$ 8.25 Hz)
δ (P*Me*)	2.36 (d, $^{2}J_{PH}$ 10.26 Hz)	2.57 (d, $^{2}J_{PH}$ 9.57 Hz)
δ (N*Me*)	2.97 (br s)	2.97 (br s)
δ (N*Me*)	3.42 (m)	3.41 (m)
δ (C*H*Me)	4.79 (q, $^{3}J_{HH}$ 6.81 Hz, $^{4}J_{PH}$ 13.6 Hz)	4.78 (q, $^{3}J_{HH}$ 6.81 Hz, $^{4}J_{PH}$ 13.6 Hz)
δ (γ*H*)	6.85 (d of d, $^{3}J_{HH}$ 6.69 Hz, $^{4}J_{PH}$ 13.98 Hz)	7.35 (m)
δ (*aromatics*)	7.28-8.50 (m)	7.38-8.46 (m)

2.2.6 $^{31}P\{^{1}H\}$ NMR Spectra of [SP-4-3]-(S_P,*S*)- and [SP-4-3]-(S_P,*S*)-73

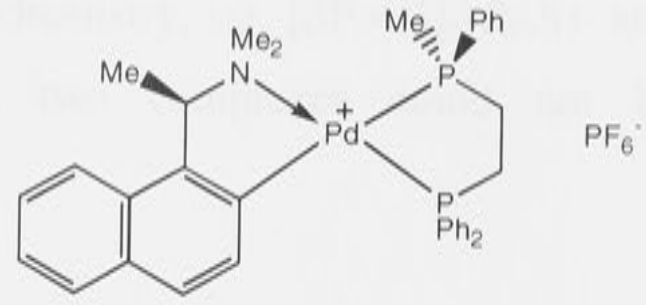
The $^{31}P\{^{1}H\}$ NMR spectrum of [SP-4-3]-(S_P,*S*)-**73** in d_6-acetone, contained a pair of doublets at δ 22.3 and 38.0 for the *P*Me$_2$ and *P*Me(C_6H_4Cl-2) groups, respectively, consistent with the presence of a single diastereomer. Likewise, the $^{31}P\{^{1}H\}$ NMR spectrum of [SP-4-3]-(R_P,*S*)-**73** in d_6-acetone exhibited a pair of doublets at δ 21.0 and 37.6 for the *P*Me$_2$ and *P*Me(C_6H_4Cl-2) groups, respectively.

The $^{31}P\{^{1}H\}$ NMR spectrum of the original mixture of four diastereomeric hexafluorophosphate salts *viz*. [SP-4-3]-(R_P,*S*)-, [SP-4-3]-(S_P,*S*)-, [SP-4-4]-(R_P,*S*)- and [SP-4-4]-(S_P,*S*)-**73**, in the same solvent, contained two other pairs of doublet resonances at δ 28.9 and 34.8, and δ 29.5 and 34.6, corresponding to [SP-4-4]-(R_P,*S*)- and [SP-4-4]-(S_P,*S*)-**73**. As separation of [SP-4-4]-(R_P,*S*)- and [SP-4-4]-(S_P,*S*)-**73** could not be achieved, an unambiguous assignment of these resonances to a particular diastereomer was not possible. $^{31}P\{^{1}H\}$ NMR chemical shift data for these complexes

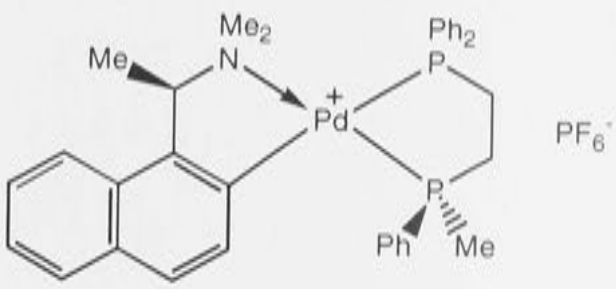
and the related diastereomeric palladium(II) salts derived from (*R*)-**72** and the chiral di(tertiary phosphine) (±)-1-(diphenylphosphino)-2-(methylphenylphosphino)ethane [(±)-**61**][113] (Figure 12) is shown in Table 5.



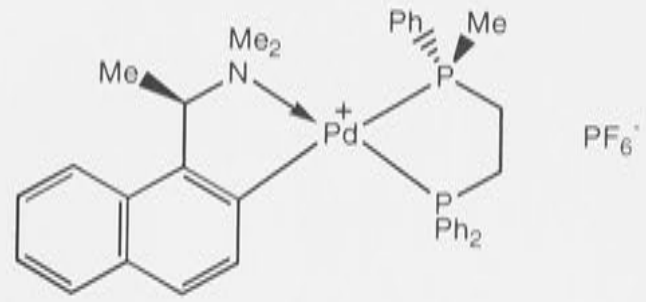
[SP-4-4]-(*R*p,*R*)-**75**



[SP-4-3]-(*R*p,*R*)-**75**



[SP-4-4]-(*S*p,*R*)-**75**



[SP-4-3]-(*S*p,*R*)-**75**

Figure 12 The four diastereomeric palladium(II) salts [SP-4-4]-(*R*p,*R*)-, [SP-4-4]-(*S*p,*R*)-, [SP-4-3]-(*R*p,*R*)- and [SP-4-3]-(*S*p,*R*)-**75**.

Table 5 Comparison of $^{31}P\{^{1}H\}$ NMR data for the diastereomeric palladium(II) salts **73** and **75**, in d_6-acetone.

Complex **73**			Complex **75**		
	δ PMe_2	δ $PMe(C_6H_4Cl\text{-}2)$		δ PMePh	δ PPh_2
[SP-4-3]-(*R*p,*S*)-	21.0 (d)	37.6 (d)	[SP-4-3]-(*S*p,*R*)-	31.3 (d)	63.2 (d)
[SP-4-3]-(*S*p,*S*)-	22.3 (d)	38.1 (d)	[SP-4-3]-(*R*p,*R*)-	29.6 (d)	63.4 (d)
[SP-4-4]-(*R*p,*S*)-	29.5 (d)	34.6 (d)	[SP-4-4]-(*S*p,*R*)-	44.7 (d)	54.1 (d)
[SP-4-4]-(*S*p,*S*)-	28.9 (d)	34.8 (d)	[SP-4-4]-(*R*p,*R*)-	44.5 (d)	48.3 (d)

Similar chemical shift data was observed for each pair of complexes with the same regiochemistry, for example, [SP-4-3]-(*R*p,S)- and [SP-4-3]-(*S*p,S)-**73**. For this reason the data could not be used to differentiate between complexes with the same regiochemistry but different configurations at the stereogenic phosphorus centre. In

the case of complex **75** two diastereomerically pure complexes were isolated with different regiochemistry, namely [SP-4-3]- and [SP-4-4]-(R_P,*R*)-**75**, and hence $^{31}P\{^1H\}$ NMR spectroscopy could be used to identify the remaining two diastereomers. In the present work, two diastereomerically pure complexes were again isolated, however, they had the same regiochemistry, *viz.* [SP-4-3]-(R_P,S)- and [SP-4-3]-(S_P,S)-**73**, and hence the remaining two complexes could not be differentiated in this way.

Chapter Three

Results and Discussion (II)

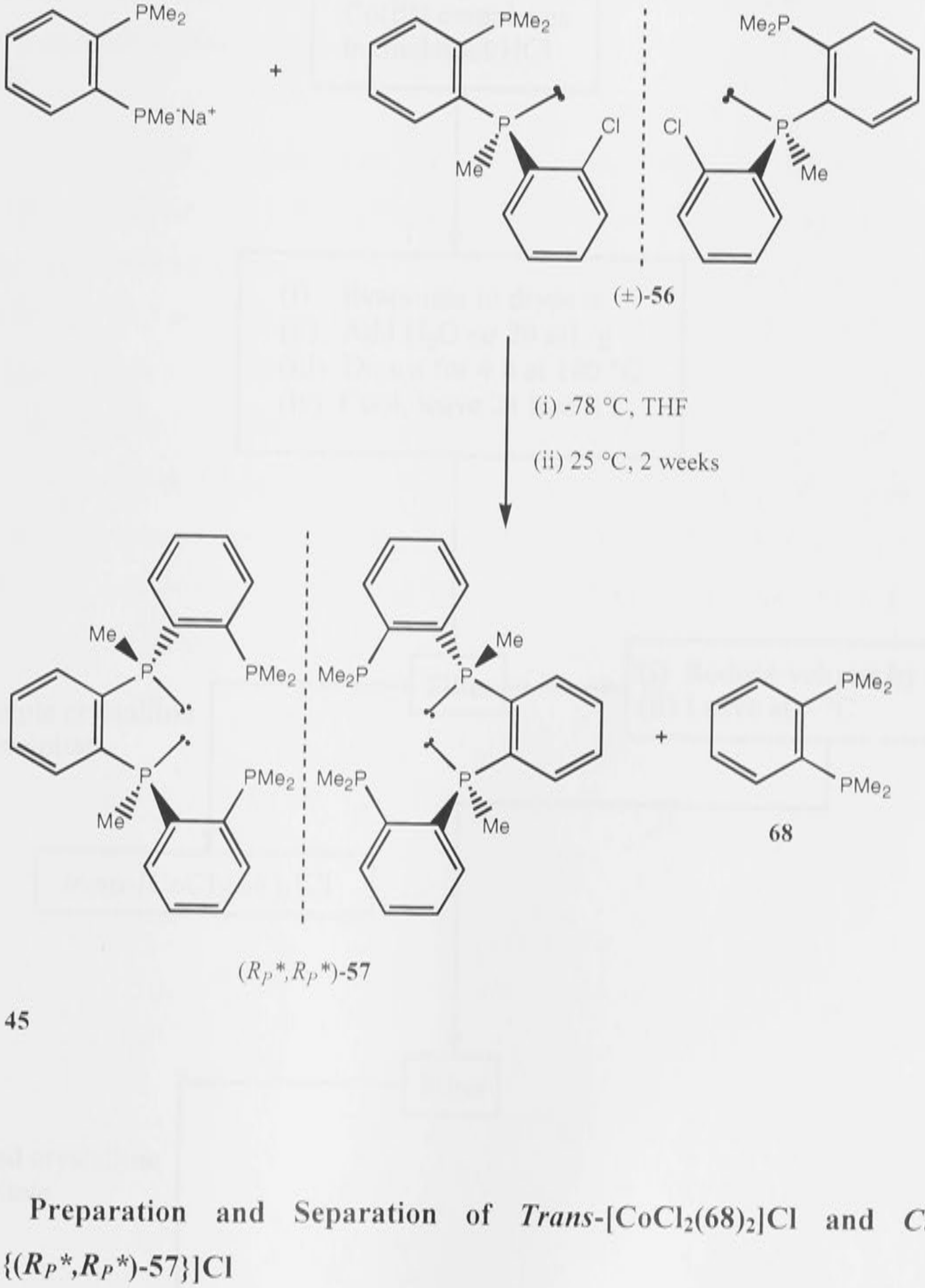
Stereoselective Synthesis and Co-ordination Chemistry of Chiral Tetra(Tertiary Phosphines)

3.1 STEREOSELECTIVE SYNTHESIS OF CHIRAL TETRA(TERTIARY PHOSPHINES)

3.1.1 Synthesis of (R_P*,R_P*)-1,2-Bis[(2-dimethylphosphinophenyl)-methylphosphino]benzene [(R_P*,R_P*)-57]

The chiral tetra(tertiary phosphine) (R_P*,R_P*)-1,2-bis[(2-dimethylphosphinophenyl)-methylphosphino]benzene [(R_P*,R_P*)-**57**] was prepared by the addition of sodium (2-dimethylphosphinophenyl)methylphosphide [generated *in situ* from the reaction of a *ca* 4:1 mixture of the secondary phosphine (±)-(2-dimethylphosphinophenyl)-methylphosphine [(±)-**66**] and 1,2-phenylenebis(dimethylphosphine) (**68**) with sodium in THF] to a solution of (±)-(2-chlorophenyl)(2-dimethylphosphinophenyl)methyl-phosphine [(±)-**56**] in THF, at -78 °C (Scheme 45). The reaction mixture was stirred for 7 days at room temperature, by which time the colour of the reaction mixture had changed from dark red to pale yellow.

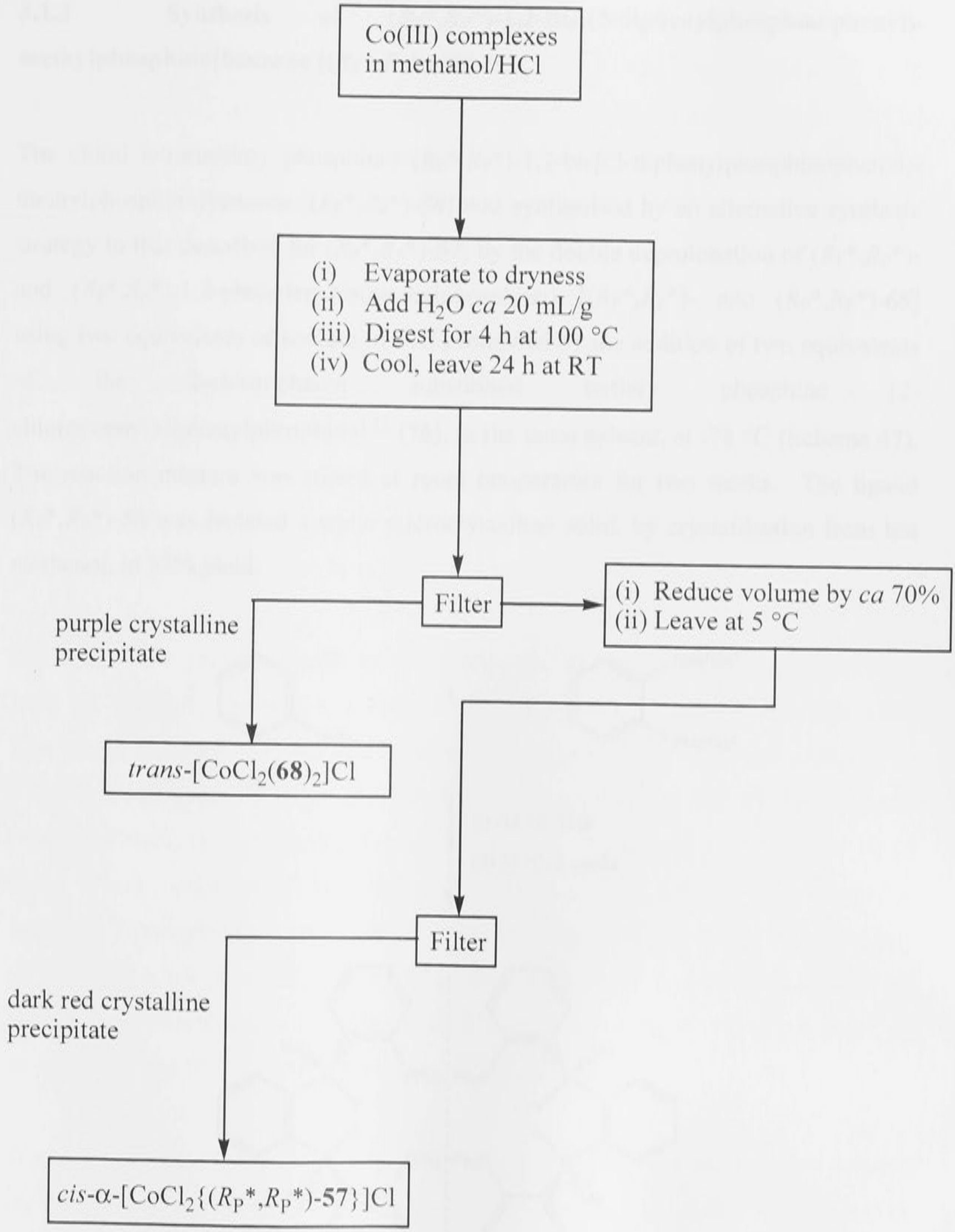
The crude product from the reaction mixture was isolated as a clear oil and white solid. The $^{31}P\{^1H\}$ NMR spectrum of the crude product in d_6-benzene revealed a major singlet resonance for the di(tertiary phosphine) **68** at δ -54.8, as well as multiplet resonances in the region δ -54.2 to -53.0 and δ -39.2 to -38.0, consistent with the presence of the tetra(tertiary phosphine) (R_P*,R_P*)-**57**. The spectrum also contained several minor resonances corresponding to unreacted (±)-**56**, secondary phosphine (±)-**66** and heterocycle **69** (which was present in (±)-**56** as an impurity, see Section 2.1.5). The mass spectrum of the crude product showed a signal at m/e 442 for the M^+ peak, as well as signals at m/e 427 $(M\text{-}Me)^+$, 381 $(M\text{-}PMe_2)^+$ and 305 $(M\text{-}C_6H_4PMe_2)^+$ consistent with the presence of the tetra(tertiary phosphine) (R_P*,R_P*)-**57**. The primary components in the crude product were separated and characterised by complexation to cobalt(III).



Scheme 45

3.1.2 Preparation and Separation of *Trans*-[$CoCl_2(68)_2$]Cl and *Cis*-α-[$CoCl_2${(*R*P*,*R*P*)-57}]Cl

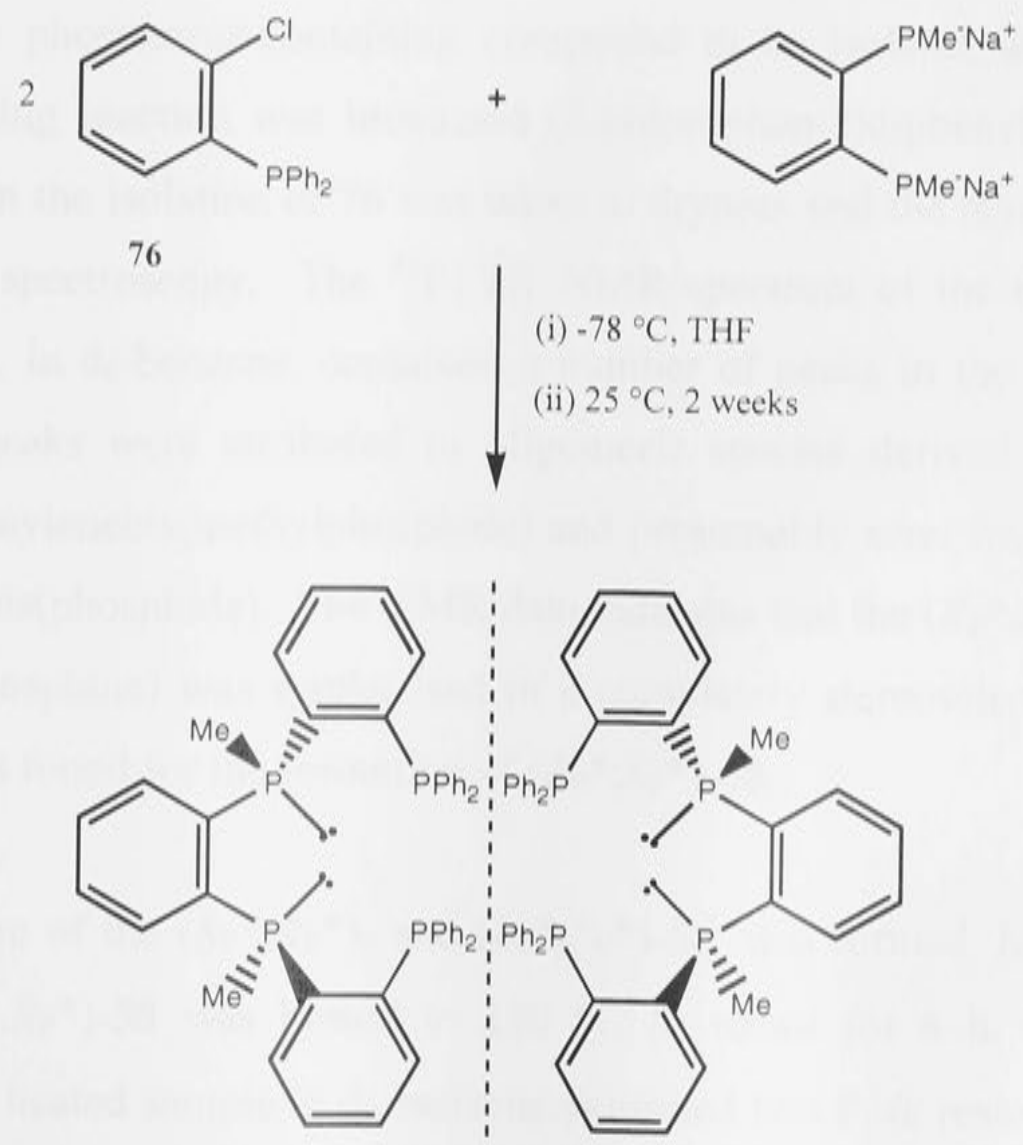
The crude product from the reaction between sodium (2-dimethylphosphinophenyl)methylphosphide and (±)-**56** was dissolved in hot methanol and treated with a solution of hexaaquacobalt(II) chloride in the same solvent. The mixture was acidified with hydrochloric acid and air was drawn through the solution for 4 h. Two cobalt(III) complexes were isolated from the reaction mixture: *trans*-[$CoCl_2$(**68**)$_2$]Cl and *cis*-α-[$CoCl_2${(*R*P*,*R*P*)-**57**}]Cl. The separation of the complexes was achieved by the procedure outlined in Scheme 46.


Co(III) complexes in methanol/HCl
(i) Evaporate to dryness
(ii) Add H_2O *ca* 20 mL/g
(iii) Digest for 4 h at 100 °C
(iv) Cool, leave 24 h at RT
Filter
purple crystalline precipitate
trans-[$CoCl_2$(**68**)$_2$]Cl
(i) Reduce volume by *ca* 70%
(ii) Leave at 5 °C
Filter
dark red crystalline precipitate
cis-α-[$CoCl_2${(R_P*,R_P*)-**57**}]Cl

Scheme 46

3.1.3 Synthesis of (R_P*,R_P*)-1,2-Bis[(2-diphenylphosphinophenyl)-methylphosphino]benzene [(R_P*,R_P*)-58]

The chiral tetra(tertiary phosphine) (R_P*,R_P*)-1,2-bis[(2-diphenylphosphinophenyl)-methylphosphino]benzene [(R_P*,R_P*)-**58**] was synthesised by an alternative synthetic strategy to that described for (R_P*,R_P*)-**57**; by the double deprotonation of (R_P*,R_P*)- and (R_P*,S_P*)-1,2-phenylenebis(methylphosphine) [(R_P*,R_P*)- and (R_P*,R_P*)-**65**] using two equivalents of sodium in THF, followed by the addition of two equivalents of the 2-chlorophenyl substituted tertiary phosphine (2-chlorophenyl)diphenylphosphine[123] (**76**), in the same solvent, at -78 °C (Scheme 47). The reaction mixture was stirred at room temperature for two weeks. The ligand (R_P*,R_P*)-**58** was isolated a white microcrystalline solid, by crystallisation from hot methanol, in 33% yield.



(R_P*,R_P*)-**58**

Scheme 47

The $^{31}P\{^{1}H\}$ NMR spectrum of (R_P*,R_P*)-**58** in d_6-benzene was consistent with that expected for an AXX'A' spin system (Figure 13). Two sets of multiplets were centered at δ -36.1 and -14.1 [$J_{AA'}$ 140.0 Hz, J_{AX} 149.5 Hz, $J_{A'X}$ 6.9 Hz, $J_{XX'}$ 0.0 Hz] for the *P*Me and *P*Ph_2 groups, respectively. A similar pattern has previously been observed for (R_P*,R_P*)-tetraphos [(R_P*,R_P*)-**38**][88] and (R_P*,R_P*)-eLTTP [(R_P*,R_P*)-**46**].[89]

The ^{1}H NMR spectrum of (R_P*,R_P*)-**58** in the same solvent consisted of a single, broad P*Me* resonance at δ 1.75, consistent with the presence of a single diastereomer (Figure 14). The mass spectrum of the product revealed a M^+ peak at 690, and a fragmentation pattern similar to that for (R_P*,R_P*)-**57**. Signals were observed at m/e 613 $(M\text{-}Ph)^+$, 505 $(M\text{-}PPh_2)^+$, and 383 $(M\text{-}C_6H_4PPh_2)^+$, consistent with the tetra(tertiary phosphine) (R_P*,R_P*)-**58**.

The only other phosphorus-containing compound to be isolated and characterised from the coupling reaction was unreacted (2-chlorophenyl)diphenylphosphine (**76**). The filtrate from the isolation of **76** was taken to dryness and the residue analysed by $^{31}P\{^{1}H\}$ NMR spectroscopy. The $^{31}P\{^{1}H\}$ NMR spectrum of the residue from the reaction filtrate, in d_6-benzene, contained a number of peaks in the region of 10-15 ppm. These peaks were attributed to oligomeric species derived from unreacted sodium 1,2-phenylenebis(methylphosphide) and presumably arise from ring cleavage of THF by the bis(phosphide). The NMR data indicates that the (R_P*,R_P*) form of the tetra(tertiary phosphine) was synthesised in a completely stereoselective manner, as no evidence was found for the formation of (R_P*,S_P*)-**58**.

A *ca* 3:1 mixture of the (R_P*,R_P*)- and (R_P*,S_P*)-**58**, was formed, however, when a sample of (R_P*,R_P*)-**58** was heated to 120 °C *in vacuo* for 6 h. The ^{1}H NMR spectrum of the heated sample in d_6-benzene exhibited two P*Me* resonances at δ 1.51 and 1.75 for (R_P*,S_P*)- and (R_P*,R_P*)-**58**, respectively, indicating epimerisation of (R_P*,R_P*)-**58** had occurred under these conditions (Figure 15).

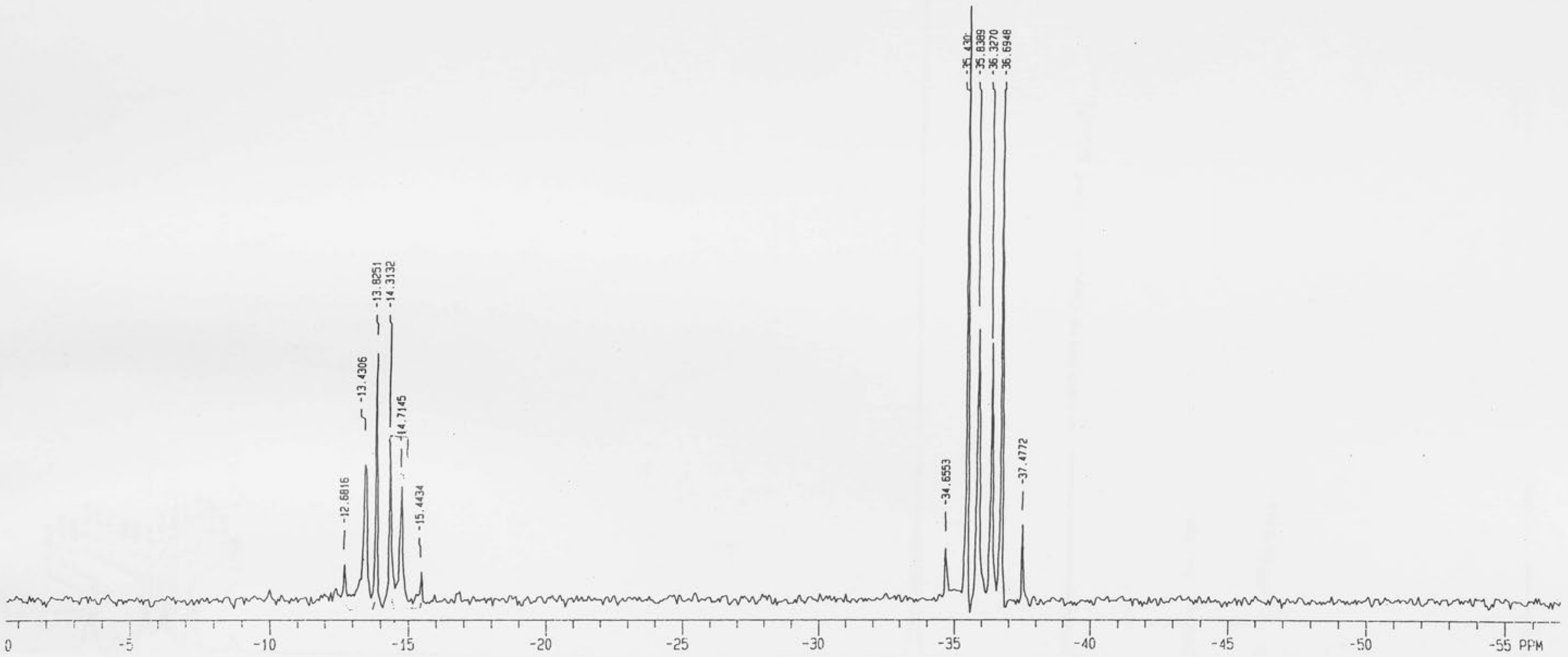


Figure 13 $^{31}P\{^{1}H\}$-NMR spectrum of (R_P*,R_P*)-**58** in d_6-benzene.

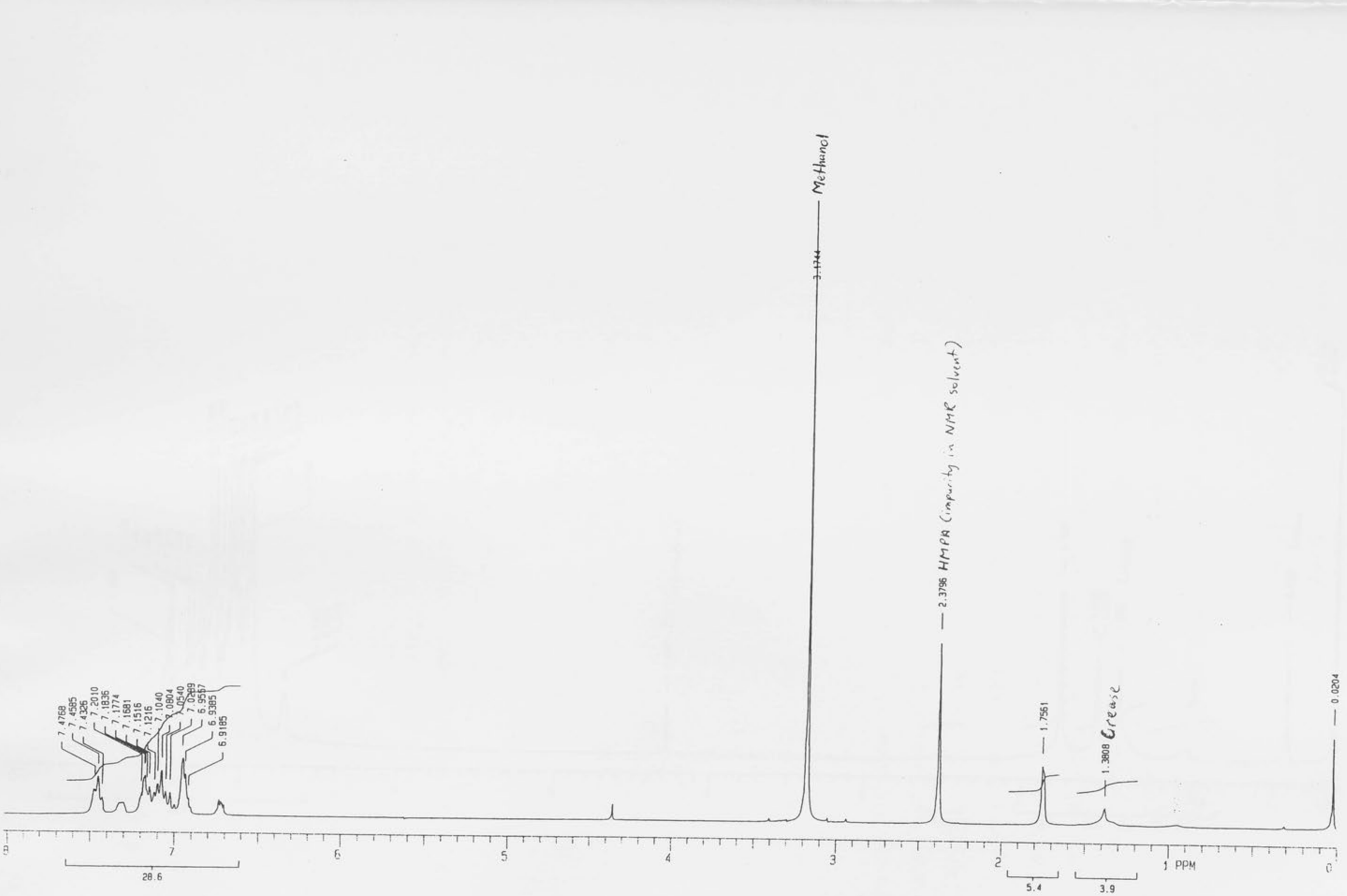


Figure 14 ^{1}H-NMR spectrum of (R_P*,R_P*)-**58** in d_6-benzene.

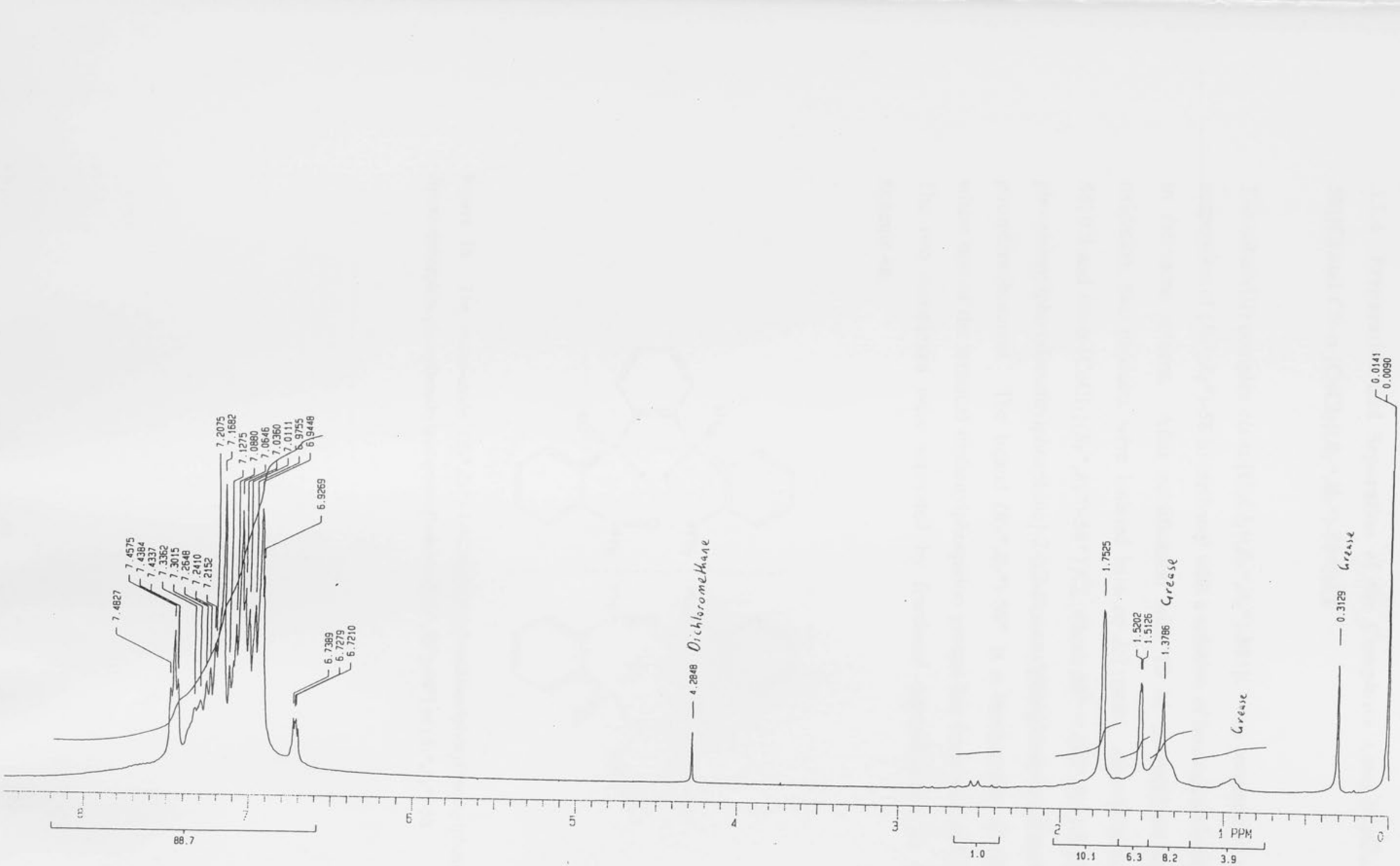


Figure 15 ^{1}H-NMR spectrum of (R_P*,R_P*)- and (R_P*,S_P*)-**58** in d_6-benzene, after heating a sample of (R_P*,R_P*)-**58** *in vacuo* at 120 °C for 6 hours.

3.1.4 Preparation and Separation of the Complexes *Cis*-α-[$CoCl_2${(R_P*,R_P*)-58}]Cl and *Cis*-α-[$CoCl_2${(R_P*,R_P*)-58*}]Cl

The cobalt(III) complex *cis*-α-[$CoCl_2${(R_P*,R_P*)-**58**}]Cl was prepared by reaction of a suspension of (R_P*,R_P*)-**58** in methanol with a solution of hexaaquacobalt(II) chloride in the same solvent. After acidification with 10 M hydrochloric acid and air oxidation, two products were isolated in a *ca* 2:1 ratio: *cis*-α-[$CoCl_2${(R_P*,R_P*)-**58**}]Cl and *cis*-α-[$CoCl_2${(R_P*,R_P*)-**58***}]Cl, where **58*** = (R_P*,R_P*)-1-[(2-diphenylphosphinoylphenyl)methylphosphino]-2-[(2-diphenylphosphinophenyl)methylphosphino]benzene. The ligand (R_P*,R_P*)-**58*** is a mono-oxide of (R_P*,R_P*)-**58**, where one of the terminal diphenylphosphino groups has been oxidised (Figure 16). The two complexes were separated by fractional crystallisation, as depicted in Scheme 48.

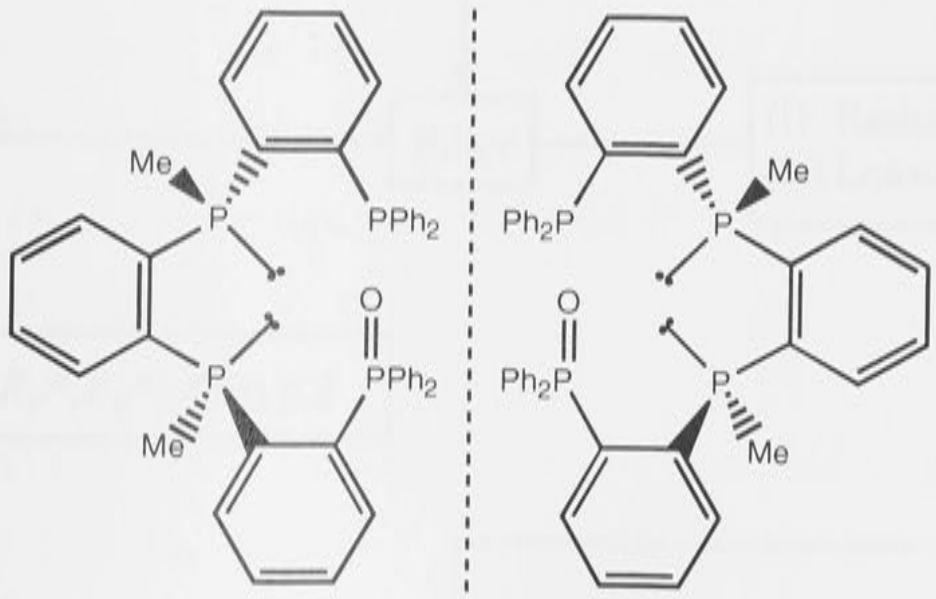
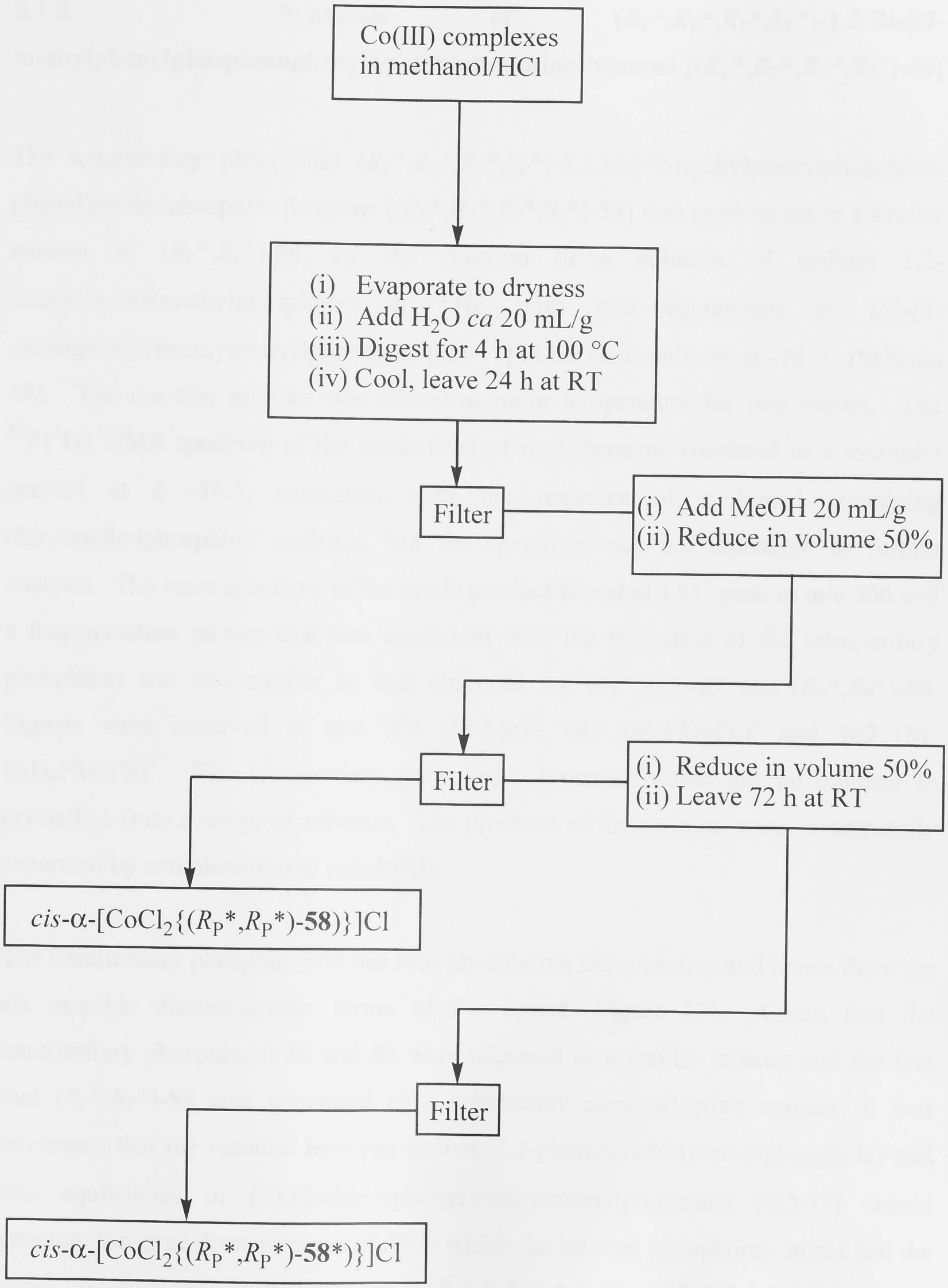


Figure 16 The mono-oxide (R_P*,R_P*)-1-[(2-diphenylphosphinoylphenyl)methylphosphino]-2-[(2-diphenylphosphinophenyl)methylphosphino]benzene [(R_P*,R_P*)-**58***] of (R_P*,R_P*)-**58**.

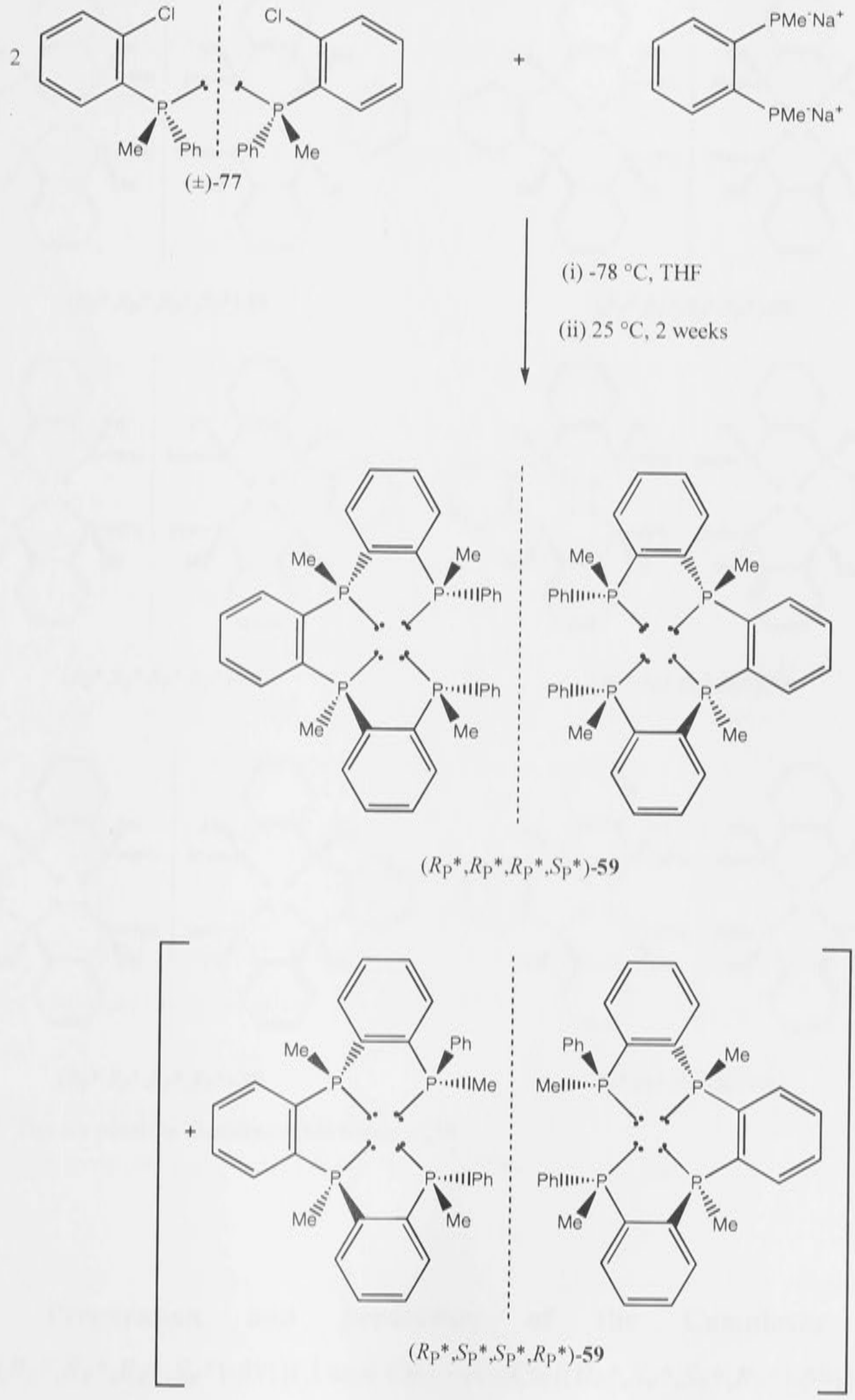

Co(III) complexes in methanol/HCl
(i) Evaporate to dryness
(ii) Add H_2O *ca* 20 mL/g
(iii) Digest for 4 h at 100 °C
(iv) Cool, leave 24 h at RT
Filter
(i) Add MeOH 20 mL/g
(ii) Reduce in volume 50%
Filter
(i) Reduce in volume 50%
(ii) Leave 72 h at RT
cis-α-[$CoCl_2${(R_P*,R_P*)-**58**)}]Cl
Filter
cis-α-[$CoCl_2${(R_P*,R_P*)-**58***)}]Cl

Scheme 48

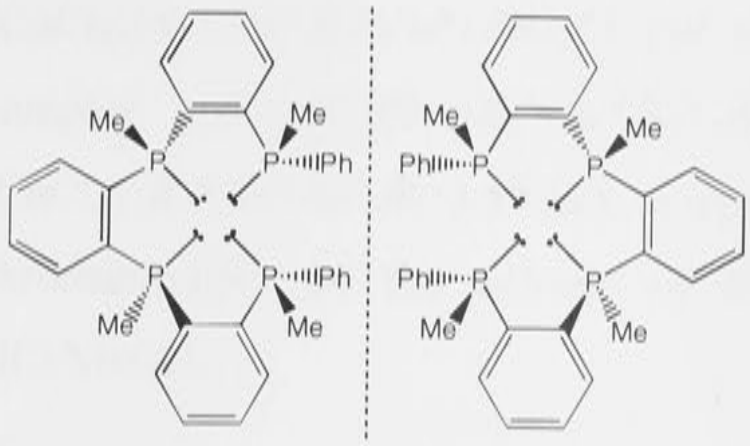
3.1.5. Synthesis of (R_P*,R_P*,R_P*,S_P*)-1,2-Bis[(2-methylphenylphosphinophenyl)methylphosphino]benzene [(R_P*,R_P*,R_P*,S_P*)-59]

The tetra(tertiary phosphine) (R_P*,R_P*,R_P*,S_P*)-1,2-bis[(2-methylphenylphosphino-phenyl)methylphosphino]benzene [(R_P*,R_P*,R_P*,S_P*)-**59**] was synthesised in a similar manner to (R_P*,R_P*)-**58**, by the reaction of a solution of sodium 1,2-phenylenebis(methylphosphide) in THF with two equivalents of (±)-(2-chlorophenyl)methylphenylphosphine [(±)-77] in the same solvent, at -78 °C (Scheme 49). The reaction mixture was stirred at room temperature for two weeks. The $^{31}P\{^1H\}$ NMR spectrum of the crude product in d_6-benzene consisted of a multiplet centred at δ -36.5, consistent with the presence of a ligand containing diarylmethylphosphino moieties, but the spectrum was not amenable to further analysis. The mass spectrum of the crude product revealed a M^+ peak at m/e 566 and a fragmentation pattern that was consistent with the formation of the tetra(tertiary phosphine) and was similar to that observed for (R_P*,R_P*)-**57** and (R_P*,R_P*)-**58**. Signals were observed at m/e 551 $(M\text{-}Me)^+$, 443 $(M\text{-}PMePh)^+$ and 367 $(M\text{-}C_6H_4PMePh)^+$. The tetra(tertiary phosphine), however, could not be induced to crystallise from a range of solvents. The products of the reaction were subsequently separated by complexation to cobalt(III).

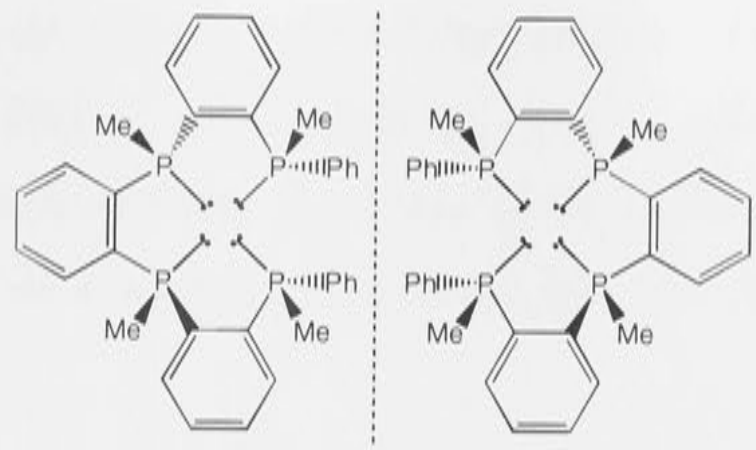
The tetra(tertiary phosphine) **59** has four phosphorus stereocentres and hence there are six possible diastereomeric forms of the ligand (Figure 17). Given that the tetra(tertiary phosphines) **58** and **59** were prepared in a similar manner and the fact that (R_P*,R_P*)-**58** was generated in a completely stereoselective manner, it was envisaged that the reaction between sodium 1,2-phenylenebis(methylphosphide) and two equivalents of (±)-(2-chlorophenyl)methylphenylphosphine [(±)-77] would generate the three diastereomers of **59** in which the internal phosphorus atoms had the same relative configuration, *viz.* (R_P*,R_P*,R_P*,R_P*)-, (R_P*,S_P*,S_P*,R_P*)- and (R_P*,R_P*,R_P*,S_P*)-**59**.


2
Cl
Cl
P
P
Me
Ph
Ph
Me
(±)-77
PMe⁻Na⁺
PMe⁻Na⁺
+
(i) -78 °C, THF
(ii) 25 °C, 2 weeks
Me
Me
P
P
Ph
P
P
Ph
Me
Me
(R_P*,R_P*,R_P*,S_P*)-59
+
Me
Ph
P
P
Me
P
P
Ph
Me
Me
Ph
Me
P
P
Me
Ph
P
P
Me
Me
(R_P*,S_P*,S_P*,R_P*)-59

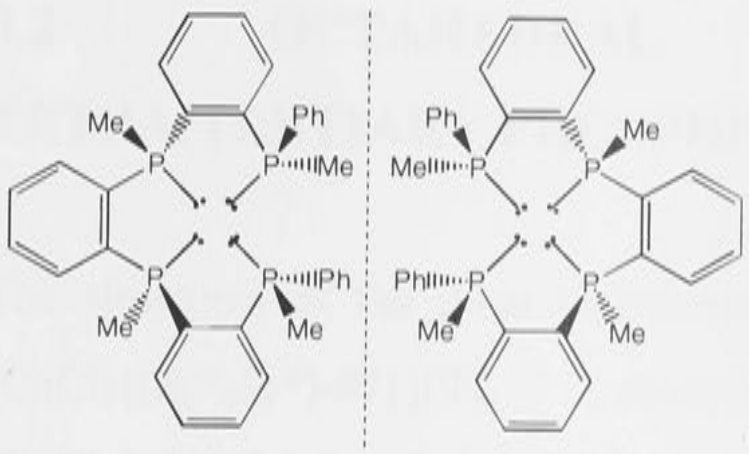
Scheme 49



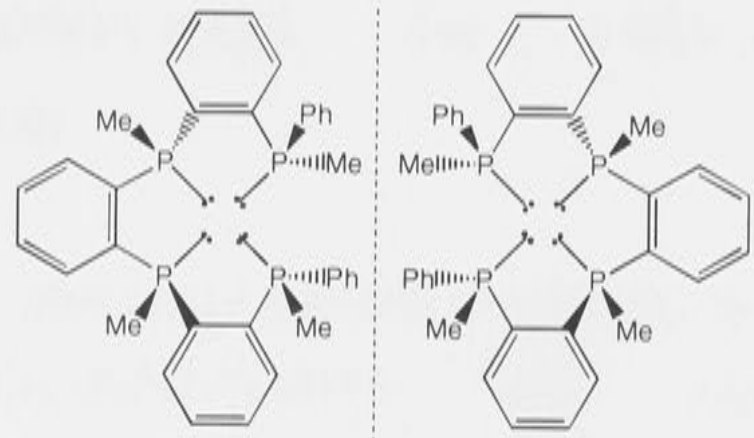
(R_P*,R_P*,R_P*,S_P*)-**59**



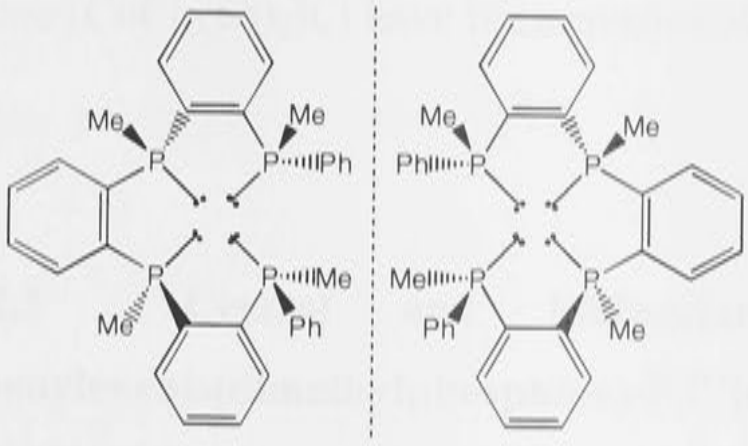
(R_P*,R_P*,S_P*,S_P*)-**59**



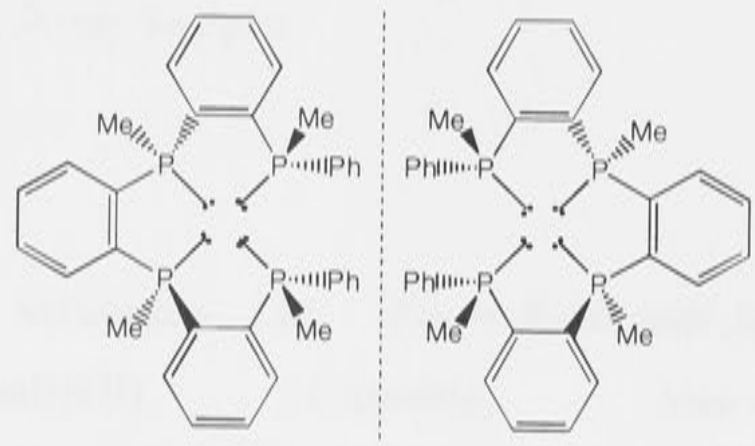
(R_P*,S_P*,S_P*,R_P*)-**59**



(R_P*,S_P*,R_P*,R_P*)-**59**



(R_P*,R_P*,R_P*,R_P*)-**59**



(R_P*,S_P*,R_P*,S_P*)-**59**

Figure 17 The six possible diastereomeric forms of **59**.

3.1.6 Preparation and Separation of the Complexes *Cis*-α-[$CoCl_2${(R_P*,R_P*,R_P*,S_P*)-59}]Cl and *Cis*-α-[$CoCl_2${(R_P*,S_P*,S_P*,R_P*)-59}]Cl

The crude product from the reaction of sodium 1,2-phenylenebis(methylphosphide) and (±)-(2-chlorophenyl)methylphenylphosphine was dissolved in methanol and the resulting solution was treated with a solution of hexaaquacobalt(II) chloride in the same solvent to give, after acidification with 10 M hydrochloric acid and air oxidation, a *ca* 9:1 mixture of the diastereomeric cobalt(III) complexes *cis*-α-

[$CoCl_2${(R_P*,R_P*,R_P*,S_P*)-**59**}]Cl and *cis*-α-[$CoCl_2${(R_P*,S_P*,S_P*,R_P*)-**59**}]Cl. The complex *cis*-α-[$CoCl_2${(R_P*,R_P*,R_P*,S_P*)-**59**}]Cl was separated from *cis*-α-[$CoCl_2${(R_P*,S_P*,S_P*,R_P*)-**59**}]Cl, in a diastereomerically pure form, by ion-exchange chromatography of the mixture of the *cis*-α complexes, eluting with 0.075M HCl/MeOH.

3.2 OCTAHEDRAL COMPLEXES OF CHIRAL TETRA(TERTIARY PHOSPHINES)

The structures of the three [tetra(tertiary phosphine)]cobalt(III) complexes *cis*-α-[$CoCl_2${(R_P*,R_P*)-**57**}]PF_6, *cis*-α-[$CoCl_2${(R_P*,R_P*)-**58**}]Cl and *cis*-α-[$CoCl_2${(R_P*,R_P*,R_P*,S_P*)-**59**}]PF_6; the related cobalt(III) complex *cis*-α-[$CoCl_2${(R_P*,R_P*)-**58***}]Cl; and the bis[di(tertiary phosphine)]cobalt(III) complex *trans*-[$CoCl_2$(**68**)$_2$]Cl have been confirmed by X-ray analyses.

3.2.1 Crystal and Molecular Structure of *Trans*-dichloro[1,2-phenylenebis(dimethylphosphine)-P,P']cobalt(III) Chloride, *trans*-[$CoCl_2$(**68**)$_2$]Cl, and [OC-6-22-(R_P*,R_P*)]-dichloro{1,2-bis[(2-dimethylphosphinophenyl)methyl-phosphino]benzene-P,P',P'',P'''}cobalt(III) Hexafluorophosphate, *cis*-α-[$CoCl_2${(R_P*,R_P*)-**57**}]PF_6

Suitable crystals of *trans*-[$CoCl_2$(**68**)$_2$]Cl for X-ray analysis were obtained by recrystallisation of the complex from methanol. Selected crystallographic data is shown in Tables 6 and 7. The molecular structure of the cation *trans*-[$CoCl_2$(**68**)$_2$]$^+$ is shown in Figure 18.

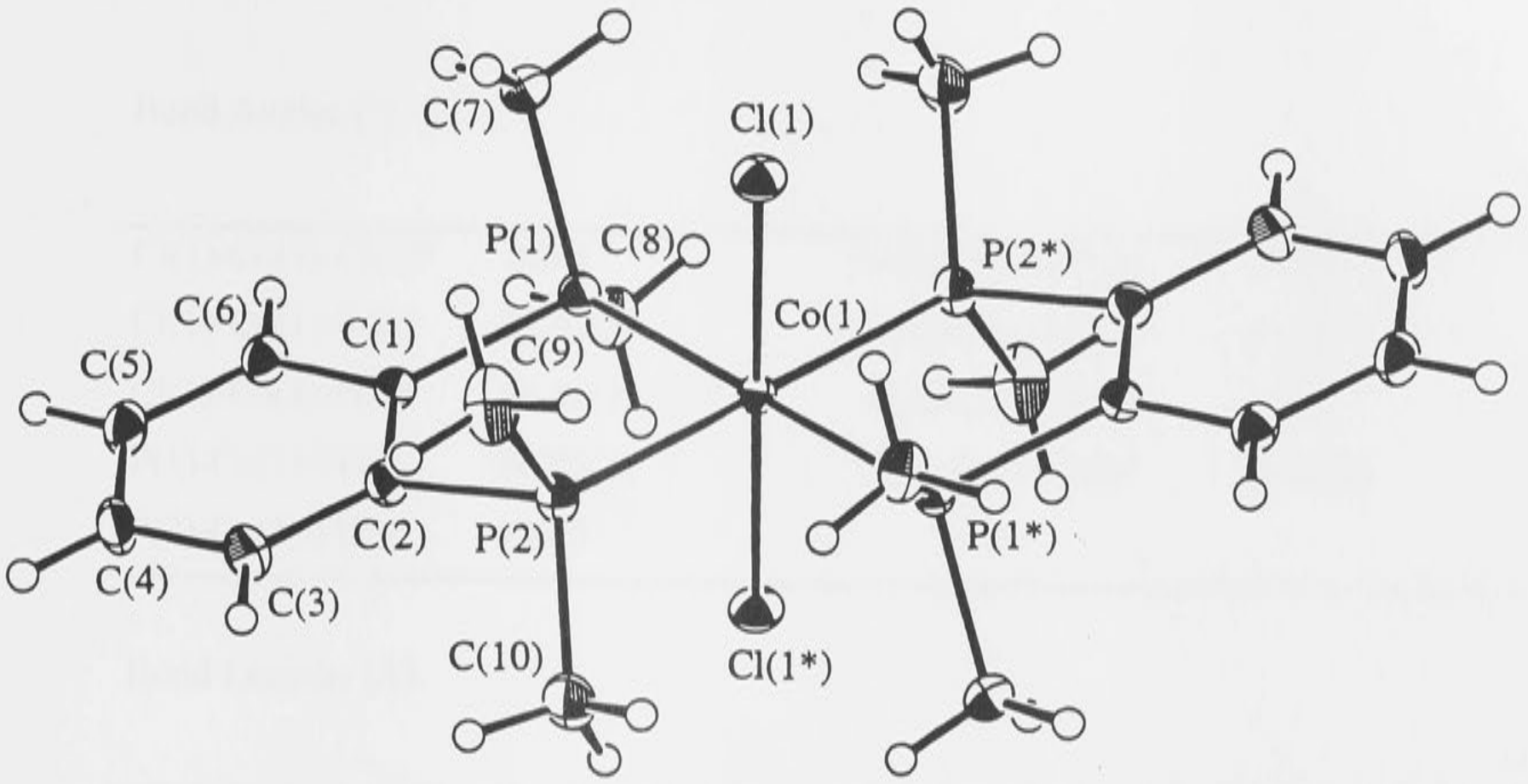


Figure 18 Molecular Structure of the cation *trans*-$[CoCl_2(\mathbf{68})_2]^+$.

Table 6 Selected crystallographic data for the complex *trans*-$[CoCl_2(\mathbf{68})_2]Cl$.

Crystal System	Monoclinic
Lattice Type	Primitive
Space Group	P21/c (#14)
Lattice Parameters	a = 9.064(2) Å b = 9.467(2) Å c = 14.727(2) Å β = 98.26(1)° V = 1250.7(3) Å^3

Table 7 Selected bond angles and bond lengths for the complex *trans*-$[CoCl_2(\mathbf{68})_2]Cl$.

Bond Angles (°)

Cl(1)-Co(1)-Cl(1)*	180.0	Cl(1)-Co(1)-P(1)	92.38(2)
Cl(1)-Co(1)-P(1)*	87.62(2)	Cl(1)-Co(1)-P(2)	93.18(3)
Cl(1)-Co(1)-P(2)*	86.82(3)	P(1)-Co(1)-P(1)*	180.0
P(1)-Co(1)-P(2)	86.05(2)	P(1)-Co(1)-P(2)*	93.95(2)
P(2)-Co(1)-P(2)*	180.0		

Bond Lengths (Å)

Co(1)-Cl(1)	2.256 (6)	Co(1)-Cl(1)*	2.256 (6)
Co(1)-P(1)	2.249 (7)	Co(1)-P(1)*	2.249 (6)
Co(1)-P(2)	2.253 (6)	Co(1)-P(2)*	2.253 (6)

* indicates atom transformed by symmetry operations (-x,-y,-z)

The X-ray structure of *trans*-$[CoCl_2(\mathbf{68})_2]ClO_4$ has previously been solved and the Co-Cl and Co-P bond lengths associated with the cation were published as part of a detailed investigation into the co-ordination chemistry of **68** and the analogous di(tertiary arsine) 1,2-phenylenebis(dimethylarsine) (diars) by Warren and Bennett.[124] However, no other crystallographic data was given or subsequently published in a separate article. The bond lengths determined here are in close agreement with that published in the previous work. The structural data showed the compound to be an octahedral bis(bidentate)cobalt(III) complex, with two chloro ligands arranged in a *trans* configuration completing the octahedral coordination sphere of the cobalt(III) centre. The structural data is very similar to that reported for the analogous complex *trans*-$[CoCl_2(diars)_2]ClO_4$.[125]

The complex *cis*-α-$[CoCl_2\{(R_P{*},R_P{*})\text{-}\mathbf{57}\}]Cl$ was converted to the corresponding hexafluorophosphate salt by metathesis with ammonium hexafluorophosphate in

methanol. Suitable crystals of *cis*-α-[$CoCl_2$\{(R_P*,R_P*)-**57**\}]PF_6 for X-ray analysis were grown from methyl ethyl ketone. The molecular structure of the cation *cis*-α-[$CoCl_2$\{(R_P*,R_P*)-**57**\}]$^+$ is shown in Figure 19, and selected crystallographic data, bond lengths and angles are given in Tables 8 and 9.

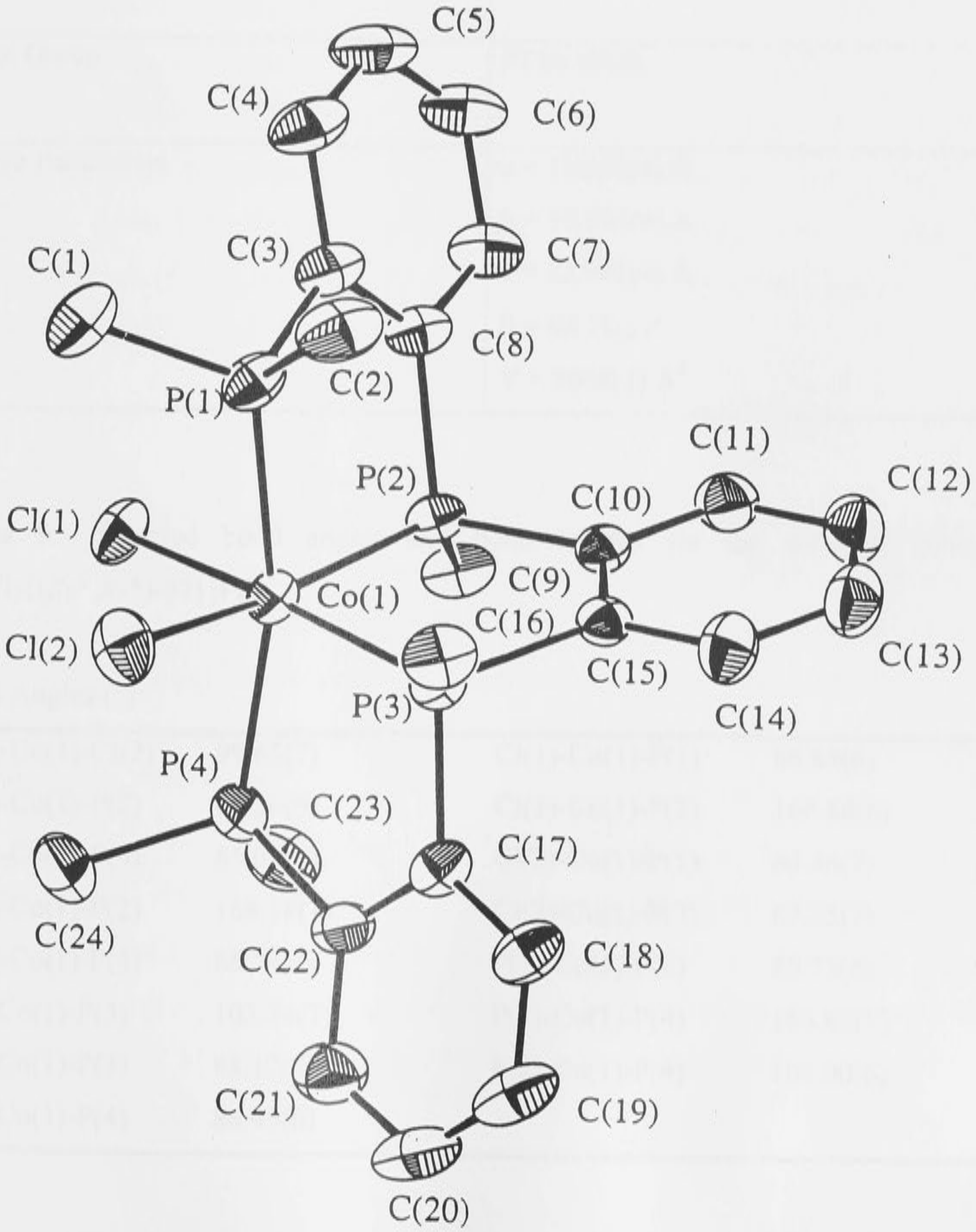


Figure 19 Molecular structure of the cation *cis*-α-[$CoCl_2$\{(R_P*,R_P*)-**57**\}]$^+$.

Table 8 Selected crystallographic data for the complex *cis*-α-[$CoCl_2$\{(R_P*,R_P*)-**57**\}]PF_6.

Crystal System	Monoclinic
Lattice Type	Primitive
Space Group	P21/a (#14)
Lattice Parameters	a = 12.630(4) Å b = 19.034(4) Å c = 12.745(4) Å β = 95.75(2)° V = 3048(1) Å^3

Table 9 Selected bond angles and bond lengths for the complex *cis*-α-[$CoCl_2$\{(R_P*,R_P*)-**57**\}]PF_6.

Bond Angles (°)

Cl(1)-Co(1)-Cl(2)	99.65(7)	Cl(1)-Co(1)-P(1)	86.88(6)
Cl(1)-Co(1)-P(2)	86.36(6)	Cl(1)-Co(1)-P(3)	168.88(6)
Cl(1)-Co(1)-P(4)	85.03(6)	Cl(2)-Co(1)-P(1)	84.46(7)
Cl(2)-Co(1)-P(2)	168.18(7)	Cl(2)-Co(1)-P(3)	87.55(7)
Cl(2)-Co(1)-P(4)	86.74(7)	P(1)-Co(1)-P(2)	85.73(6)
P(1)-Co(1)-P(3)	102.34(7)	P(1)-Co(1)-P(4)	166.89(7)
P(2)-Co(1)-P(3)	88.12(6)	P(2)-Co(1)-P(4)	104.00(6)
P(3)-Co(1)-P(4)	86.95(6)		

Bond Lengths (Å)

Co(1)-Cl(1)	2.314(2)	Co(1)-Cl(2)	2.270(2)
Co(1)-P(1)	2.243(2)	Co(1)-P(2)	2.176(2)
Co(1)-P(3)	2.173(2)	Co(1)-P(4)	2.248(2)

The complex *cis*-α-[$CoCl_2${(R_P*,R_P*)-**57**}]PF_6 is a racemic compound with both Δ-(S_P,S_P) and Λ-(R_P,R_P) forms of the cation being present in the unit cell. Only the Δ-(S_P,S_P) form is shown in Figure 19. The structural data clearly shows that the ligand has adopted a *cis*-α geometry about the metal ion and that the two stereogenic phosphorus atoms have the same relative configuration, indicating that the coupling reaction between (±)-**56** and sodium (2-dimethylphosphinophenyl)methylphosphide to generate (R_P*,R_P*)-**57** was completely stereoselective.

3.2.2 Crystal and Molecular Structure of [OC-6-22-(R_P*,R_P*)]-Dichloro{1,2-bis[(2-diphenylphosphinophenyl)methylphosphino]benzene-P,P',P'',P'''}cobalt-(III) Chloride, *cis*-α-[$CoCl_2${(R_P*,R_P*)-58}]Cl and [OC-6-22-(R_P*,R_P*)]-Dichloro{1,2-bis{[1-(2-diphenylphosphinoylphenyl)-2-(2-diphenylphosphino-phenyl)]methylphosphino}-benzene-O,P,P',P''}cobalt(III) Chloride, *cis*-α-[$CoCl_2${(R_P*,R_P*)-58*}]Cl

Suitable crystals of both *cis*-α-[$CoCl_2${(R_P*,R_P*)-**58**}]Cl and *cis*-α-[$CoCl_2${(R_P*,R_P*)-**58***}]Cl were obtained from methanol and their structures were determined by X-ray crystallography. Selected crystallographic data for the two complexes are shown in Tables 10 and 11. Molecular structures of the two cations are shown in Figures 20 and 21.

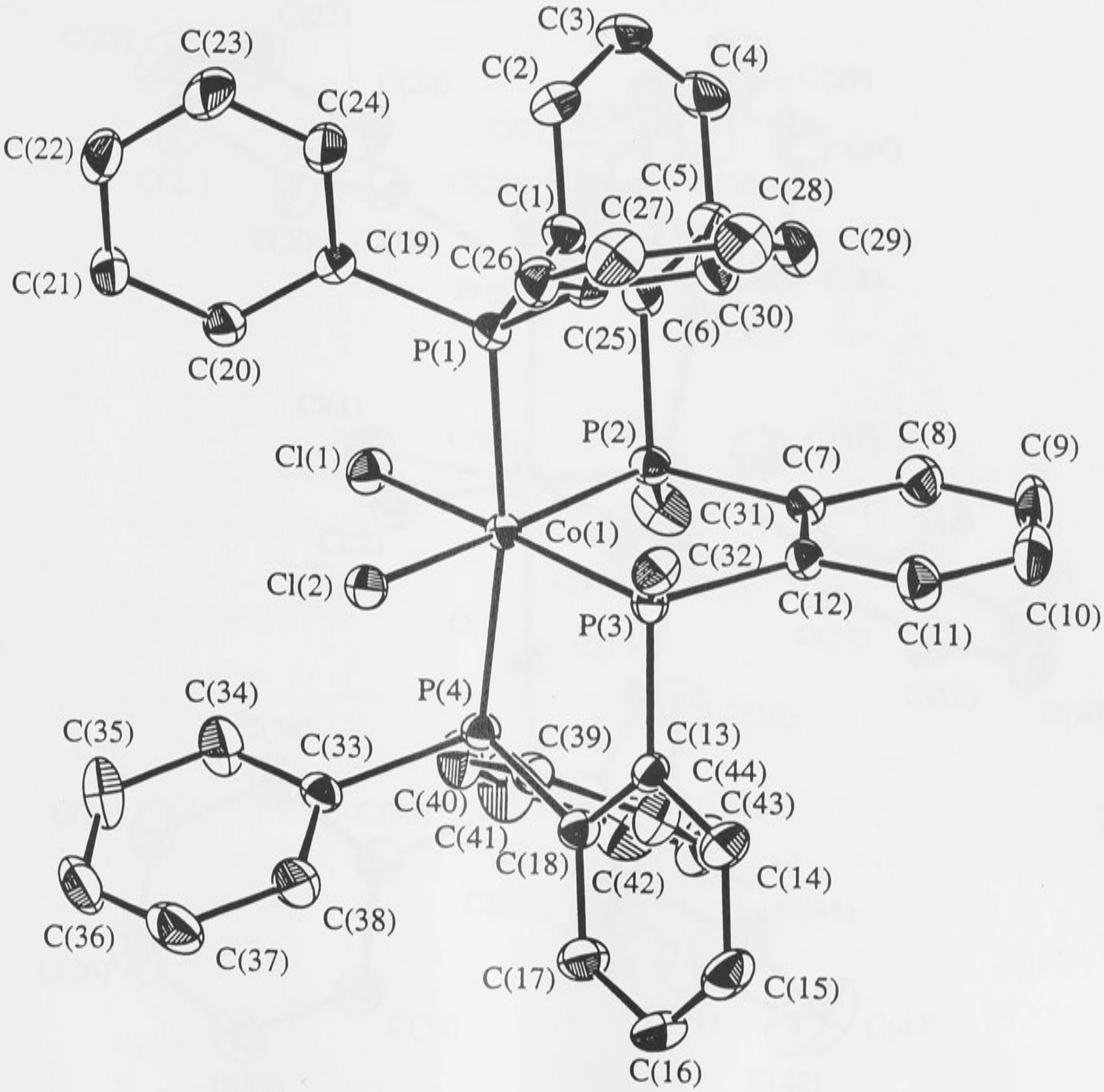


Figure 20 Molecular structure of *cis*-α-$[CoCl_2\{(R_P^*,R_P^*)$-**58**$\}]^+$.

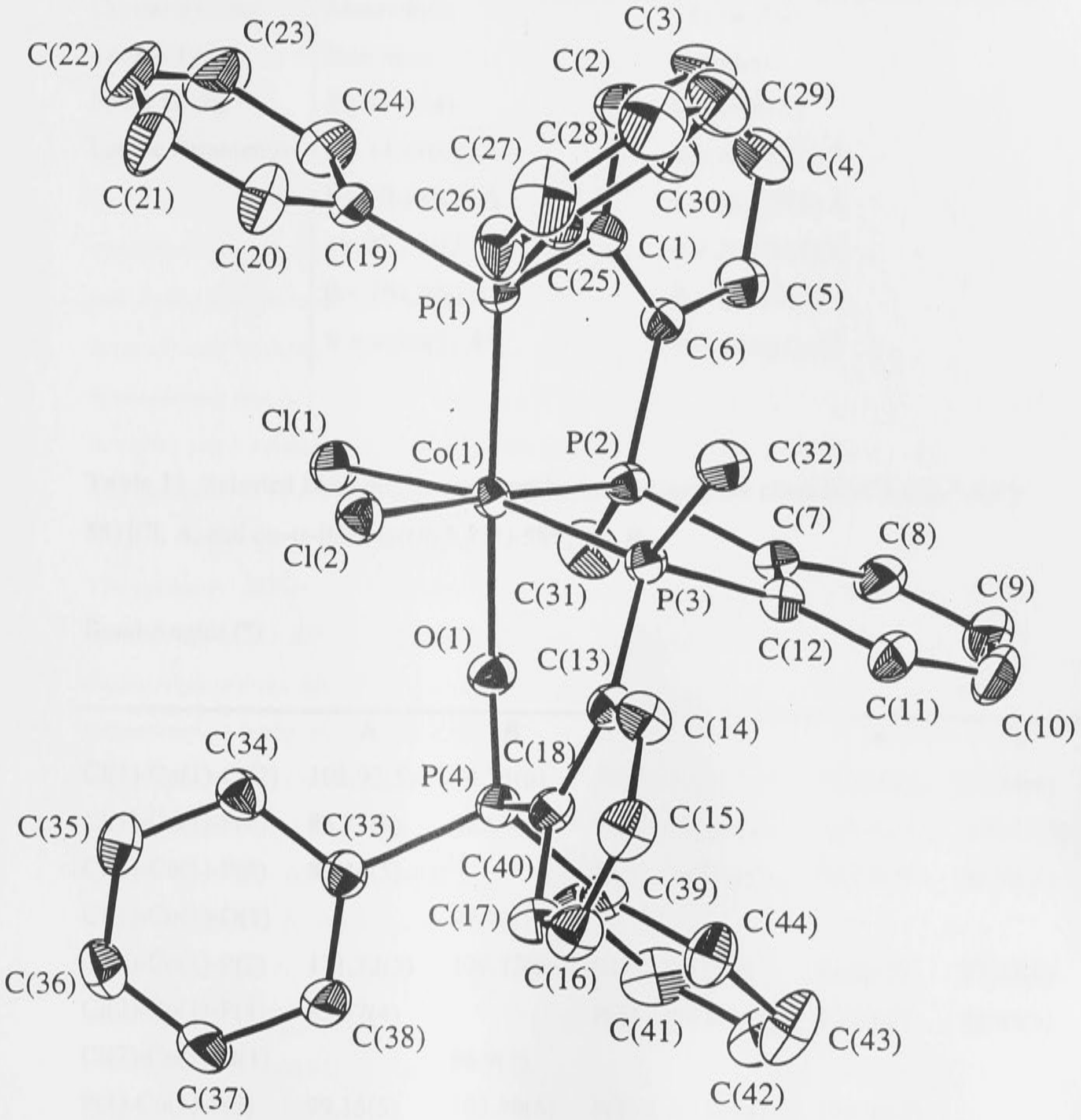


Figure 21 Molecular structure of *cis*-α-[$CoCl_2${(R_P*,R_P*)-**58***}]$^+$.

Table 10 Selected crystallographic data for the complexes *cis*-α-[$CoCl_2$\{(R_P*,R_P*)-**58**\}]Cl, **A**, and *cis*-α-[$CoCl_2$\{(R_P*,R_P*)-**58***\}]Cl, **B**.

	A	**B**
Crystal System	Monoclinic	Monoclinic
Lattice Type	Primitive	Primitive
Space Group	P21/c (#14)	P21/c (#14)
Lattice Parameters	a = 14.110(3) Å	a = 16.781(2) Å
	b = 12.159(3) Å	b = 13.870(2) Å
	c = 25.263(3) Å	c = 20.316(3) Å
	β = 104.29(1)°	β = 110.27(1)°
	V = 4200(2) Å^3	V = 4436(1) Å^3

Table 11 Selected bond angles and lengths for the complex *cis*-α-[$CoCl_2$\{(R_P*,R_P*)-**58**\}]Cl, **A**, and *cis*-α-[$CoCl_2$\{(R_P*,R_P*)-**58***\}]Cl, **B**

Bond Angles (°)

	A	**B**		**A**	**B**
Cl(1)-Co(1)-Cl(2)	102.92(5)	94.73(6)	Cl(1)-Co(1)-P(1)	87.54(5)	92.84(6)
Cl(1)-Co(1)-P(2)	83.77(5)	88.89(6)	Cl(1)-Co(1)-P(3)	169.97(5)	169.47(6)
Cl(1)-Co(1)-P(4)	87.44(5)		Cl(2)-Co(1)-P(1)	88.36(5)	86.92(6)
Cl(1)-Co(1)-O(1)		97.7(1)			
Cl(2)-Co(1)-P(2)	171.32(5)	176.22(6)	Cl(2)-Co(1)-P(3)	84.85(5)	87.37(6)
Cl(2)-Co(1)-P(4)	85.37(4)		P(1)-Co(1)-P(2)	86.39(5)	88.44(6)
Cl(2)-Co(1)-O(1)		86.9(1)			
P(1)-Co(1)-P(3)	99.15(5)	103.30(6)	P(1)-Co(1)-P(4)	170.90(5)	
			P(1)-Co(1)-O(1)		168.2(1)
P(2)-Co(1)-P(3)	89.16(5)	88.88(6)	P(2)-Co(1)-P(4)	100.59(5)	
P(3)-Co(1)-P(4)	86.87(5)		P(2)-Co(1)-O(1)		84.1(1)
P(3)-Co(1)-O(1)		82.6(1)	Co(1)-O(1)-P(4)		143.7(4)

Bond Lengths (Å)

	A	B		A	B
Co(1)-Cl(1)	2.302(1)	2.283(2)	Co(1)-Cl(2)	2.284(1)	2.265(1)
Co(1)-P(1)	2.282(1)	2.211(2)	Co(1)-P(2)	2.186(1)	2.165(2)
Co(1)-P(3)	2.185(1)	2.216(1)	Co(1)-P(4)	2.280(1)	
			Co(1)-O(1)		1.989(3)

The complexes *cis*-α-[$CoCl_2${(R_P*,R_P*)-**58**}]Cl and *cis*-α-[$CoCl_2${(R_P*,R_P*)-**58***}]Cl are structurally very similar. They are both racemic compounds, with the Δ-(R_P,R_P) and Λ-(S_P,S_P) forms of the cation being present in the unit cell (only the Δ-(R_P,R_P) form of each is shown). It is clear from the structural data that in both cases the *cis*-α diastereomer has been formed exclusively and the two stereogenic phosphorus atoms have the same relative configuration, indicating that the (R_P*,R_P*) diastereomer of **58** was synthesised in a completely stereoselective manner.

The primary difference between the two structures is that in the case of *cis*-α-[$CoCl_2${(R_P*,R_P*)-**58***}]Cl an oxygen atom has been inserted between a terminal diphenylphosphino group and the metal centre. A similar effect has been reported for ruthenium(II) complexes of 1,2-phenylenebis(methylphenylarsine), where insertion of an oxygen atom into a Ru-As bond was confirmed by X-ray crystallography.[126] There is little structural information concerning mixed phosphine-phosphine oxide ligands co-ordinated to cobalt(III). The Co(1)-O(1) and P(4)-O(1) bond lengths of 1.989 and 1.491 Å, respectively, are very similar to previously reported values of 1.984 and 1.499 Å, respectively, for a cobalt(II) complex containing a Co-O-P bond sequence.[127] Oxygen insertion is believed to occur during the air oxidation of cobalt(II) to cobalt(III), particularly since similar treatment of a solution of *cis*-α-[$CoCl_2${(R_P*,R_P*)-**58**}]Cl in methanol did not result in conversion to *cis*-α-[$CoCl_2${(R_P*,R_P*)-**58***}]Cl.

3.2.3 Crystal and Molecular Structure of [OC-6-22-(R_P*,R_P*,R_P*,S_P*)]-Dichloro{1,2-bis[(2-methylphenylphosphinophenyl)methylphosphino]benzene-P,P',P'',P'''}cobalt(III) Hexafluorophosphate, *cis*-α-[$CoCl_2${(R_P*,R_P*,R_P*,S_P*)-**59**}]PF_6

The chloride salt *cis*-α-[$CoCl_2${(R_P*,R_P*,R_P*,S_P*)-**59**}]Cl was converted to the hexafluorophosphate salt *cis*-α-[$CoCl_2${(R_P*,R_P*,R_P*,S_P*)-**59**}]PF_6 by metathesis with aqueous ammonium hexafluorophosphate in methanol. Suitable crystals of the complex for X-ray analysis were grown by slow diffusion of propan-2-ol into a solution of the complex in dichloromethane. Selected crystallographic data for the complex is given in Table 12 and bond lengths and angles in Table 13. The molecular structure of the cation *cis*-α-[$CoCl_2${(R_P*,R_P*,R_P*,S_P*)-**59**}]$^+$ is shown in Figure 22.

Table 12 Selected crystallographic data for the complex *cis*-α-[$CoCl_2${(R_P*,R_P*,R_P*,S_P*)-**59**}]PF_6.

Crystal System	Triclinic
Lattice Type	Primitive
Space Group	$P\bar{1}$ (#2)
Lattice Parameters	a = 10.032(3) Å b = 11.198(4) Å c = 19.503(7) Å α = 104.423(2)° β = 95.608(2)° γ = 109.436(2)° V = 1965.5(1) Å^3

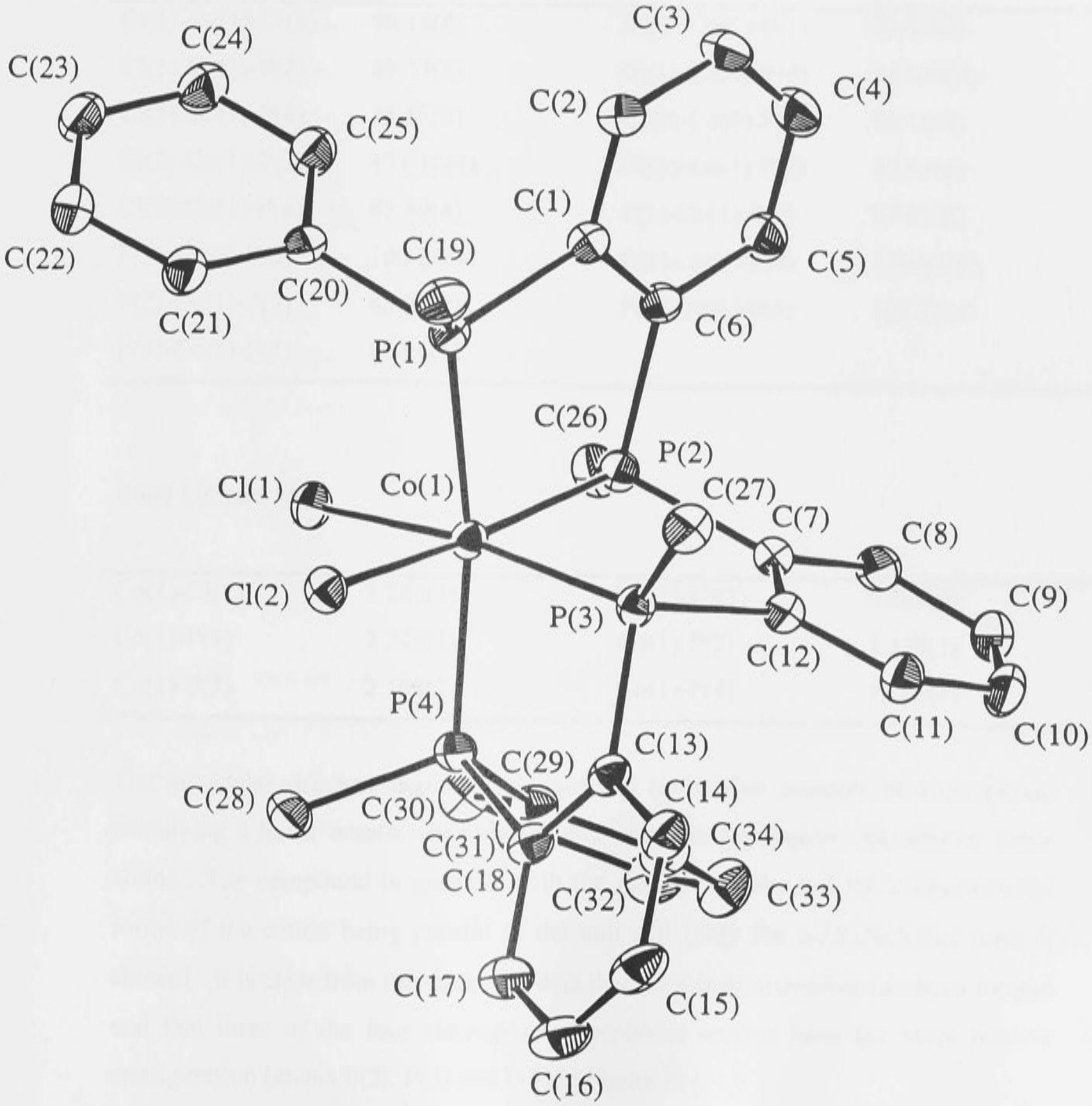


Figure 22 Molecular structure of *cis*-α-$[CoCl_2\{(R_P*,R_P*,R_P*,S_P*)\text{-}\mathbf{59}\}]^+$.

Table 13 Selected bond angles and bond lengths for the complex *cis*-α-[$CoCl_2$\{(R_P*,R_P*,R_P*,S_P*)-**59**\}]PF_6

Bond Angles (°)

Cl(1)-Co(1)-Cl(2)	96.16(4)	Cl(1)-Co(1)-P(1)	91.12(4)
Cl(1)-Co(1)-P(2)	89.57(4)	Cl(1)-Co(1)-P(3)	167.52(4)
Cl(1)-Co(1)-P(4)	85.57(4)	Cl(2)-Co(1)-P(1)	86.15(4)
Cl(2)-Co(1)-P(2)	171.16(4)	Cl(2)-Co(1)-P(3)	89.78(4)
Cl(2)-Co(1)-P(4)	85.49(4)	P(1)-Co(1)-P(2)	87.01(4)
P(1)-Co(1)-P(3)	100.25(4)	P(1)-Co(1)-P(4)	170.62(4)
P(2)-Co(1)-P(3)	85.93(4)	P(2)-Co(1)-P(4)	101.71(4)
P(3)-Co(1)-P(4)	83.96(4)		

Bond Lengths (Å)

Co(1)-Cl(1)	2.285(1)	Co(1)-Cl(2)	2.282(9)
Co(1)-P(1)	2.248(1)	Co(1)-P(2)	2.178(1)
Co(1)-P(3)	2.198(1)	Co(1)-P(4)	2.255(1)

The molecular structure depicted in Figure 22 is the first example of a compound containing a linear tetra(tertiary phosphine) with four stereogenic phosphorus donor atoms. The compound is racemic, with the Λ-(R_P,R_P,R_P,S_P) and the Δ-(R_P,S_P,S_P,S_P) forms of the cation being present in the unit cell [only the Δ-(R_P,S_P,S_P,S_P) form is shown]. It is clear from the structural data that a *cis*-α diastereomer has been formed and that three of the four stereogenic phosphorus centres have the same relative configuration [atoms P(2), P(3) and P(4) in Figure 22].

The structural data for the [tetra(tertiary phosphine)]cobalt(III) complexes *cis*-α-[$CoCl_2$\{(R_P*,R_P*)-**57**\}]PF_6, *cis*-α-[$CoCl_2$\{(R_P*,R_P*)-**58**\}]Cl and *cis*-α-[$CoCl_2$\{(R_P*,R_P*,R_P*,S_P*)-**59**\}]PF_6 are very similar. All three complexes have a distorted octahedral geometry, as indicated by the angle subtended by the terminal

phosphorus atoms and the metal centre [P(1)-Co-P(4)] which ranges between 166.89 - 176.02° for the three complexes. The angles of the three metal chelate rings are also similar for each complex, and range between 85.73 - 87.01° for P(1)-Co-P(2), 85.73 - 89.16° for P(2)-Co-P(3), and 83.96 - 86.95° for P(3)-Co-P(4).

The Co-P bond lengths for the three [tetra(tertiary phosphine)]cobalt(III) complexes are similar to the Co-P bond lengths of 2.19 and 2.23 Å for the complex $[(triphos)Co(As_2S)]BF_4.C_6H_6$, [triphos = 1,1,1-tris(diphenylphosphinomethyl)-ethane[128] and 2.26 Å for the cobalt(III) complex *trans*-$[CoCl_2(dmpe)_2]ClO_4$ [dmpe = 1,2-bis(dimethylphosphino)ethane].[129] It is noteworthy, however, that the bond lengths between the terminal phosphorus donors and cobalt(III) (which range between 2.24 - 2.28 Å) are longer than those for the internal phosphorus atoms and the metal centre (2.17 - 2.20 Å) in all three [tetra(tertiary phosphine)]cobalt(III) complexes prepared in this work.

3.2.4 NMR Spectra of [Tetra(Tertiary Phosphine)]Cobalt(III) Complexes

The NMR spectra of the [tetra(tertiary phosphine)]cobalt(III) complexes *cis*-α-$[CoCl_2\{(R_P^*,R_P^*)$-**57**$\}]PF_6$, *cis*-α-$[CoCl_2\{(R_P^*,R_P^*)$-**58**$\}]Cl$ and *cis*-α-$[CoCl_2\{(R_P^*,R_P^*,R_P^*,S_P^*)$-**59**$\}]PF_6$; the related complex *cis*-α-$[CoCl_2\{(R_P^*,R_P^*)$-**58***$\}]Cl$; and the bis[di(tertiary phosphine)]cobalt(III) compound *trans*-$[CoCl_2($**68**$)_2]Cl$, can be rationalised in terms of their solid state structures. Selected NMR data for these cobalt(III) complexes and *cis*-α-$[CoCl_2\{(R_P^*,R_P^*,R_P^*,S_P^*)$-**59**$\}]Cl$ is given in Table 14.

Table 14 Selected ^{1}H and $^{31}P\{^{1}H\}$ NMR data for the cobalt(III) complexes *trans*-$[CoCl_2(\mathbf{65})_2]Cl$ and *cis*-α-$[CoCl_2L]X$ (L = **57, 58, 58***, or **59** and X = Cl or PF_6).

	^{1}H NMR		$^{31}P\{^{1}H\}$ NMR
	δ PMe[a]	δ PMe_2 / δ PMePh	δ P[b]
trans-$[CoCl_2(\mathbf{65})_2]Cl$[c]		1.98 s	54.9
cis-α-$[CoCl_2\{(R_P*,R_P*)\text{-}\mathbf{57}\}]PF_6$[d]	2.09 t (4.2)	2.31 t (15.6)[e]	92.8, 58.7[f]
		2.43 t (15.6)[e]	
cis-α-$[CoCl_2\{(R_P*,R_P*)\text{-}\mathbf{58}\}]Cl$[g]	0.96 t (6.6)	-	90.0, 60.5
cis-α-$[CoCl_2\{(R_P*,R_P*)\text{-}\mathbf{58*}\}]Cl$[g]	0.85 d (13.6)	-	43.1[h], 46.8 m, 52.9 t, 97.2 t
	2.35 d (14.2)		
cis-α-$[CoCl_2\{(R_P*,R_P*,R_P*,S_P*)\text{-}\mathbf{59}\}]PF_6$[f]	0.85 d (12.6)	2.29 d (10.6)[a]	60.8, 88.1, 95.2
	2.49 d (8.3)		
cis-α-$[CoCl_2\{(R_P*,S_P*,S_P*,R_P*)\text{-}\mathbf{59}\}]Cl$[c]	2.18 t (3.84)	2.45 t (6.6)[a]	59.6, 92.5

[a] Coupling constants ($^{2}J_{PH}$/Hz) are given in parentheses. [b] Resonances are broad singlets unless indicated otherwise. [c] In d_4-methanol. [d] In d_6 acetone. [e] Coupling constant ($|^{2}J_{PH} + {}^{2}J_{PH}|$/Hz) is given in parentheses. [f] In d_2-dichloromethane. [g] In d_6-dimethylsulfoxide. [h] $P(O)Ph_2$ resonance

3.2.4.1 ^{1}H NMR spectra of cobalt(III) complexes

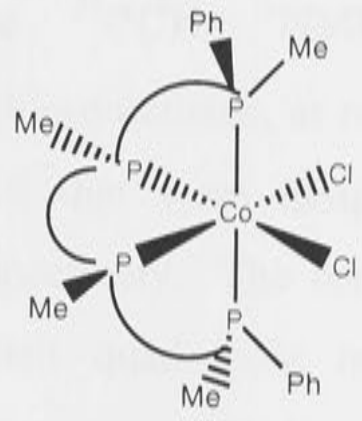
The ^{1}H NMR spectrum of *trans*-[$CoCl_2$(**68**)$_2$]Cl in d_4-methanol consisted of a singlet at δ 1.98 for the four equivalent P*Me* groups. The ^{1}H NMR spectrum of *cis*-α-[$CoCl_2${(R_P*,R_P*)-**57**}]PF_6 in d_6-acetone consisted of a multiplet at δ 2.09, attributable to the internal P*Me* groups, and two triplets at δ 2.31 and 2.43 for the diastereotopic P*Me*Me and PMe*Me* groups. The ^{1}H NMR spectrum of *cis*-α-[$CoCl_2${(R_P*,R_P*)-**58**}]Cl in d_6-dimethylsulfoxide consisted of a virtual triplet at δ 0.96 for the P*Me* resonance. The P*Me* resonance was significantly shifted upfield in comparison to the analogous PMe resonance in the ^{1}H NMR spectrum of the complex *cis*-α-[$CoCl_2${(R_P*,R_P*)-**57**}]PF_6, and can be rationalised in terms of shielding of the PMe groups in *cis*-α-[$CoCl_2${(R_P*,R_P*)-**58**}]Cl by a phenyl substituent of the terminal diphenylphosphino groups of the coordinated ligand **58**. The molecular structure of *cis*-α-[$CoCl_2${(R_P*,R_P*)-**58**}]Cl suggests that the methyl group attached to P(2) would be shielded by a phenyl substituent attached to P(4) and similarly the methyl group of P(3) would be shielded by a phenyl group of P(1) (Figure 20).

The ^{1}H NMR spectrum of the related complex *cis*-α-[$CoCl_2${(R_P*,R_P*)-**58***}]Cl in d_6-dimethylsulfoxide exhibited two doublet P*Me* resonances at δ 0.85 and 2.35. The upfield signal was assigned to the P*Me* group adjacent to the terminal $P(O)Ph_2$ moiety, and the downfield resonance to the P*Me* group adjacent to the terminal PPh_2 moiety [C(32) and C(31) in Figure 21, respectively]. The methyl group C(32) is clearly shielded by one of the two phenyl substituents attached to P(1). The insertion of an oxygen atom between the cobalt(III) centre and P(4) significantly diminishes any similar shielding effects between C(31) and a phenyl substituent of P(4).

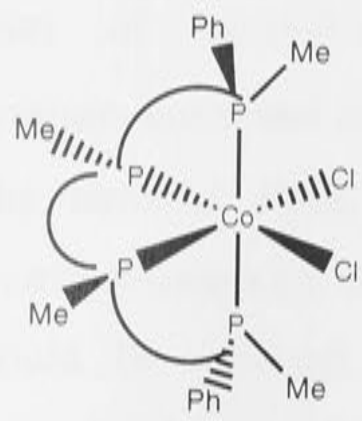
The ^{1}H NMR spectrum of *cis*-α-[$CoCl_2${(R_P*,R_P*,R_P*,S_P*)-**59**}]PF_6 in d_2-dichloromethane exhibited three P*Me* doublets at δ 0.93, 2.38 and 2.48. The two terminal P*Me* resonances were co-incident at δ 2.38, and therefore the spectrum was consistent with the C_1 symmetry of the cation. The molecular structure of *cis*-α-[$CoCl_2${(R_P*,R_P*,R_P*,S_P*)-**59**}]$^+$ (Figure 22) suggests that the methyl group attached to P(2) would be shielded by the phenyl substituent of P(4). This type of effect is not apparent for the methyl group attached to P(3). Consequently, the upfield resonance

at δ 0.93 was assigned to the methyl substituent of P(2) and the downfield resonance at δ 2.48 to the methyl substituent of P(3).

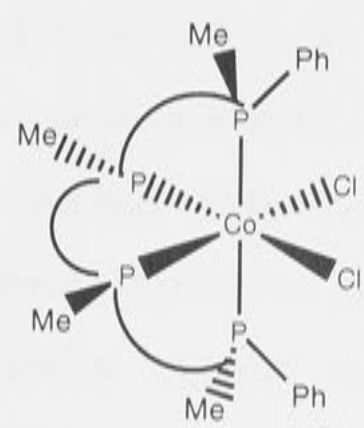
The diastereomeric cobalt(III) complex *cis*-α-[$CoCl_2$\{(R_P*,S_P*,S_P*,R_P*)-**59**\}]Cl was identified by ^{1}H NMR spectroscopy. It was assumed that the internal phosphorus stereocentres had the same relative configuration, and hence the *cis*-α diastereomer was formed exclusively upon co-ordination of the tetra(tertiary phosphine) to cobalt(III). Given this restriction, three diastereomeric cobalt(III) complexes of **59** can be envisaged, including the aforementioned complex ion *cis*-α-[$CoCl_2$\{(R_P*,R_P*,R_P*,S_P*)-**59**\}]$^+$, and these are shown in Figure 23. The ^{1}H NMR spectrum of the complex *cis*-α-[$CoCl_2$\{(R_P*,S_P*,S_P*,R_P*)-**59**\}]Cl in d_4-methanol revealed two P*Me* resonances at δ 2.18 and 2.45, consistent with the C_2 symmetry of the cation. The absence of an upfield P*Me* resonance, as was observed for *cis*-α-[$CoCl_2$\{(R_P*,R_P*,R_P*,S_P*)-**59**\}]PF_6, rules out the presence of the analogous C_2 cation *cis*-α-[$CoCl_2$\{(R_P*,R_P*,R_P*,R_P*)-**59**\}]$^+$, as for this diastereomer both internal PMe groups would be shielded by the phenyl substituent of the terminal PMePh group and hence the resonance associated with them would be shifted to higher field in the ^{1}H NMR spectrum.



(R_P*,R_P*,R_P*,S_P*)



(R_P*,R_P*,R_P*,R_P*)



(R_P*,S_P*,S_P*,R_P*)

Figure 23 The diastereomeric forms of *cis*-α-[$CoCl_2$\{**59**\}]$^+$ in which the internal phosphorus stereocentres have the same relative configuration (only one enantiomeric form of each complex is shown and the 1,2-phenylene groups have been omitted for clarity).

3.2.4.2 $^{31}P\{^{1}H\}$ NMR spectra of cobalt(III) complexes

The $^{31}P\{^{1}H\}$ NMR spectrum of *trans*-$[CoCl_2(\mathbf{68})_2]Cl$ in d_4-methanol exhibited a singlet at δ 54.9. The $^{31}P\{^{1}H\}$ NMR spectra of the [tetra(tertiary phosphine)]cobalt(III) complexes typically consisted of a broad ^{31}P resonance in the region of 40-60 ppm and another similar resonance in the region of 88-95 ppm. The downfield signal in each case was assigned to the internal phosphorus atoms of the co-ordinated ligand. A similar resonance at δ 85.0 was previously reported for the internal *P*Me group of the related As_2NP quadridentate ligand (R_{As}*,S_P*)-1-[(2-aminophenyl)methylphosphino]-2-[(2-dimethylarsinophenyl)methylarsino]benzene [(R_{As}*,S_P*)-**51**] in the $^{31}P\{^{1}H\}$ NMR spectrum of the complex *cis*-α-$[CoCl_2\{(R_{As}*,S_P*)\text{-}\mathbf{51}\}]Cl$ in d_4-methanol.[130] Furthermore, the assignment was consistent with that previously reported for the related [tetra(tertiary phosphine)]cobalt(III) complex *cis*-β-$[CoCl_2\{(R_P*,S_P*)\text{-tetraphos}\}]PF_6$. The $^{31}P\{^{1}H\}$ NMR spectrum of the complex in d_1-chloroform exhibited four ^{31}P resonances at δ 36.7, 38.7, 102.9 and 104.7. The two downfield resonances were assigned to the internal *P*Ph groups, and the upfield resonances were assigned to the terminal PPh_2 groups.[131]

The $^{31}P\{^{1}H\}$ NMR spectrum of *cis*-α-$[CoCl_2\{(R_P*,R_P*)\text{-}\mathbf{57}\}]PF_6$ in d_2-dichloromethane, at room temperature, consisted of two broad singlets at δ 58.7 and 92.8 that were assigned to the terminal PMe_2 and the internal *P*Me groups, respectively. The broad phosphorus resonances, which are strongly affected by the cobalt quadrupole moment, could be resolved into somewhat sharper singlet resonances when the spectrum was recorded at -80 °C (Figure 24).

The $^{31}P\{^{1}H\}$ NMR spectrum of *cis*-α-$[CoCl_2\{(R_P*,R_P*)\text{-}\mathbf{58}\}]Cl$ in d_6-dimethylsulfoxide revealed two broad singlet resonances at δ 60.5 and 90.0 for the terminal PPh_2 and the internal *P*Me groups, respectively. The analogous spectrum for *cis*-α-$[CoCl_2\{(R_P*,R_P*)\text{-}\mathbf{58}*\}]Cl$ in the same solvent consisted of a broad singlet at δ 43.0, two triplets at δ 97.2 and 52.9, and a multiplet at δ 46.8. The singlet ^{31}P resonance clearly corresponded to the $P(O)Ph_2$ moiety. The triplet at δ 97.2 was

assigned to P(2) (see Figure 21). This stereogenic phosphorus atom is part of two five-membered metal chelate rings and hence resides in a similar environment to that of the phosphorus stereocentres in the related complexes *cis*-α-[$CoCl_2${(R_P*,R_P*)-**58**}]Cl, *cis*-α-[$CoCl_2${(R_P*,R_P*)-**57**}]PF_6 and *cis*-α-[$CoCl_2${(R_{As}*,S_P*)-**51**}]Cl. Phosphorus atom P(2) was coupled to both P(1) and P(3) ($^2J_{PP}$ 60 Hz). The second triplet at δ 52.9 was assigned to the phosphorus atom P(1), and the multiplet to P(3) (see Figure 21). Phosphorus atom P(1) was coupled to both P(2) and P(3) ($^2J_{PP}$ 62 Hz) while P(3) was coupled to all three phosphorus atoms, hence giving rise to a multiplet resonance.

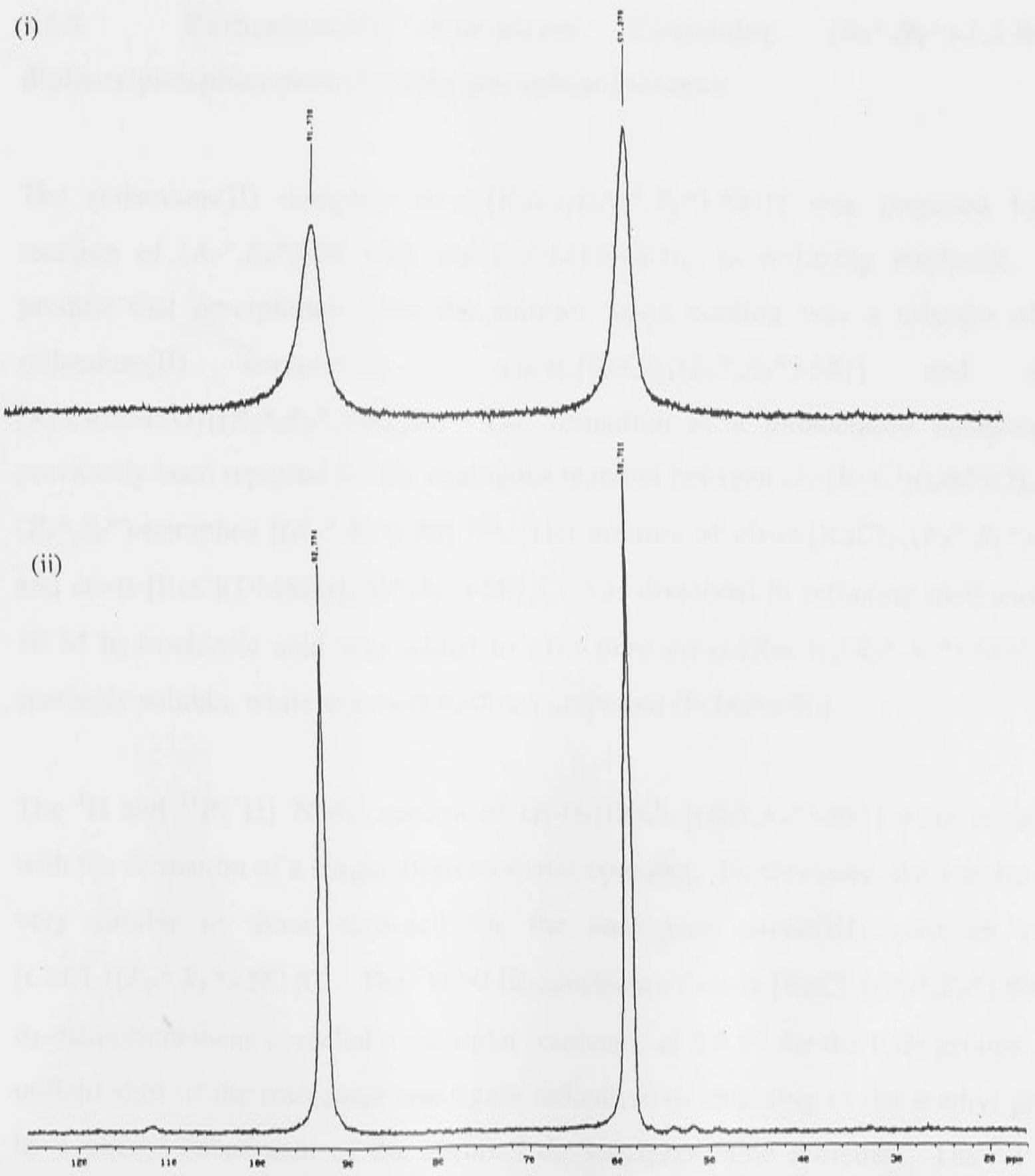


Figure 24 The $^{31}P\{^1H\}$ NMR spectrum of *cis*-α-[$CoCl_2${(R_P*,R_P*)-57}]PF_6 in d_2-dichloromethane, at (a) 25 °C and (b) -80 °C.

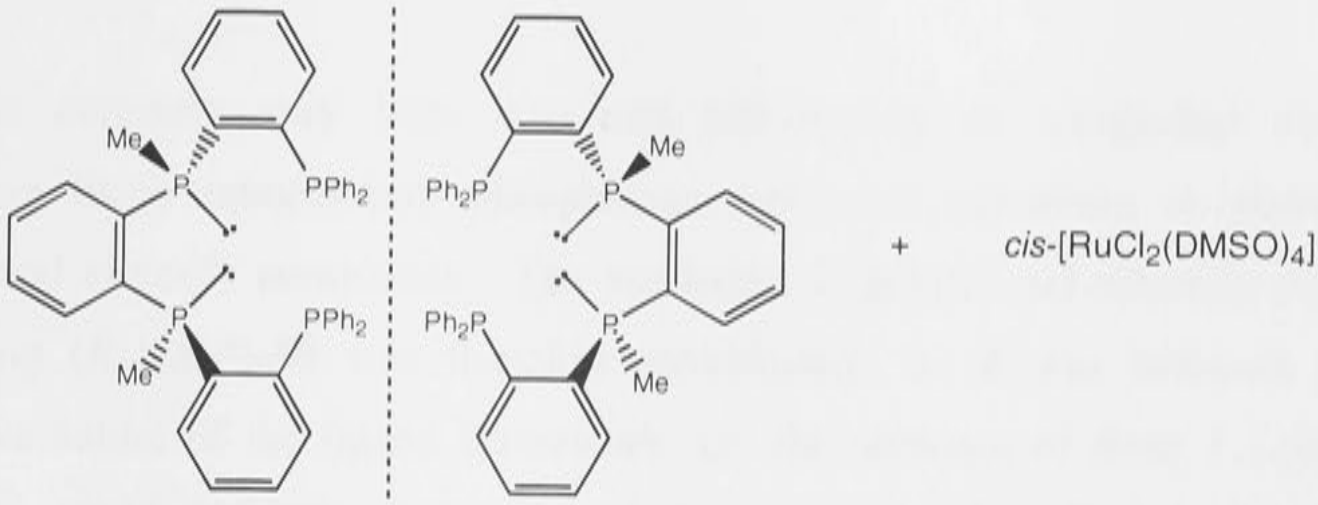
The $^{31}P\{^{1}H\}$ NMR spectrum of *cis*-α-[$CoCl_2$\{(R_P*,R_P*,R_P*,S_P*)-**59**\}]PF_6 in d_4-methanol consisted of three broad singlet resonances at δ 60.8, 88.1 and 95.3. The singlet at δ 60.8 was assigned to the terminal *P*PhMe groups, and the two other signals were assigned to the inequivalent, internal *P*Me groups. The $^{31}P\{^{1}H\}$ NMR spectrum of *cis*-α-[$CoCl_2$\{(R_P*,S_P*,S_P*,R_P*)-**59**\}]Cl in d_4-methanol consisted of two broad resonances at δ 59.6 and 92.5 for the terminal *P*PhMe and internal *P*Me groups, respectively.

3.2.5 Ruthenium(II) Complexes Containing (R_P*,R_P*)-1,2-Bis[(2-diphenylphosphinophenyl)methylphosphino]benzene

The ruthenium(II) complex *cis*-α-[$RuCl_2$\{(R_P*,R_P*)-**58**)\}] was prepared by the reaction of (R_P*,R_P*)-**58** with *cis*-[$RuCl_2(DMSO)_4$] in refluxing methanol. The product that precipitated from the solution upon cooling was a mixture of two ruthenium(II) complexes: *cis*-α-[$RuCl_2$\{(R_P*,R_P*)-**58**\}] and *cis*-α-[RuCl(DMSO)\{(R_P*,R_P*)-**58**\}]Cl. The formation of a monochloro complex has previously been reported for the analogous reaction between *cis*-[$RuCl_2(DMSO)_4$] and (R_P*,S_P*)-tetraphos [(R_P*,R_P*)-**38**].[132] The mixture of *cis*-α-[$RuCl_2$\{(R_P*,R_P*)-**58**\}] and *cis*-α-[RuCl(DMSO)\{(R_P*,R_P*)-**58**\}]Cl was dissolved in refluxing methanol and 10 M hydrochloric acid was added to give pure *cis*-α-[$RuCl_2$\{(R_P*,R_P*)-**58**\}] as a sparingly soluble, white microcrystalline compound (Scheme 50).

The ^{1}H and $^{31}P\{^{1}H\}$ NMR spectra of *cis*-α-[$RuCl_2$\{(R_P*,R_P*)-**58**\}] were consistent with the formation of a single diastereomeric complex. Furthermore, the spectra were very similar to those recorded for the analogous cobalt(III) complex *cis*-α-[$CoCl_2$\{(R_P*,R_P*)-**58**\}]Cl. The ^{1}H NMR spectrum of *cis*-α-[$RuCl_2$\{(R_P*,R_P*)-**58**\}] in d_2-dichloromethane revealed a multiplet resonance at δ 0.97 for the P*Me* groups. The upfield shift of the resonance was again indicative of shielding of the methyl groups by a phenyl substituent of the terminal diphenylphosphino moieties. The $^{31}P\{^{1}H\}$ NMR spectrum of the complex in the same solvent exhibited two sharp triplets at δ

53.2 ($^2J_{PP}$ 19.1 Hz) and 84.1 ($^2J_{PP}$ 20.6 Hz), for the terminal $P\text{Ph}_2$ and internal $P\text{Me}$ groups, respectively.



cis-α-[$RuCl_2${(R_P*,R_P)-**58**}]

[Only one enantiomer of each chiral species is shown.
The1,2-phenylene groups have also been omitted for clarity.]

Scheme 50

3.3 TETRAHEDRAL GOLD(I) AND SILVER(I) COMPLEXES OF (R_P*,R_P*)-1,2-BIS[(2-DIPHENYLPHOSPHINOPHENYL)-METHYLPHOSPHINO]BENZENE

There is currently very little structural information on tetrahedral complexes containing linear tetra(tertiary phosphines), and none pertaining to mononuclear gold(I) and silver(I) complexes. The synthesis of gold(I) and silver(I) complexes containing (R_P*,R_P*)-**58** was therefore investigated, as it was believed that the restrictive nature of the ligand framework, i.e. the presence of three 1,2-phenylene linkages, would preclude formation of any species other than a mononuclear tetrahedral complex.

3.3.1 Preparation of gold(I) and silver(I) complexes containing (R_P*,R_P*)-58

The reaction of equimolar amounts of (R_P*,R_P*)-**58** and tetrabutylammonium diiodoaurate in ethanol, followed by addition of aqueous ammonium hexafluorophosphate, gave the mononuclear gold(I) complex [Au{(R_P*,R_P*)-**58**}]PF_6 (Scheme 51). The reaction of (R_P*,R_P*)-**58** with silver nitrate in ethanol, followed by the addition of aqueous ammonium hexafluorophosphate, however, gave two silver(I) complexes: [Ag{(R_P*,R_P*)-**58**}]PF_6 and [Ag{(R_P*,R_P*)-**58**‡}]PF_6, where **58**‡ = 1,2-bis[(2-diphenylphosphinophenyl)methylphosphinoyl]benzene (Scheme 51 and Figure 25). The ligand (R_P*,R_P*)-**58**‡ is a dioxide of (R_P*,R_P*)-**58** in which the internal phosphorus atoms have been oxidised. Suitable crystals of [Ag{(R_P*,R_P*)-**58**‡}]PF_6 for an X-ray analysis were obtained by fractional crystallisation of the mixture of silver(I) complexes from acetone/propan-2-ol. A pure sample of [Ag{(R_P*,R_P*)-**58**}]PF_6, however, could not be isolated from the mixture of silver(I) complexes.

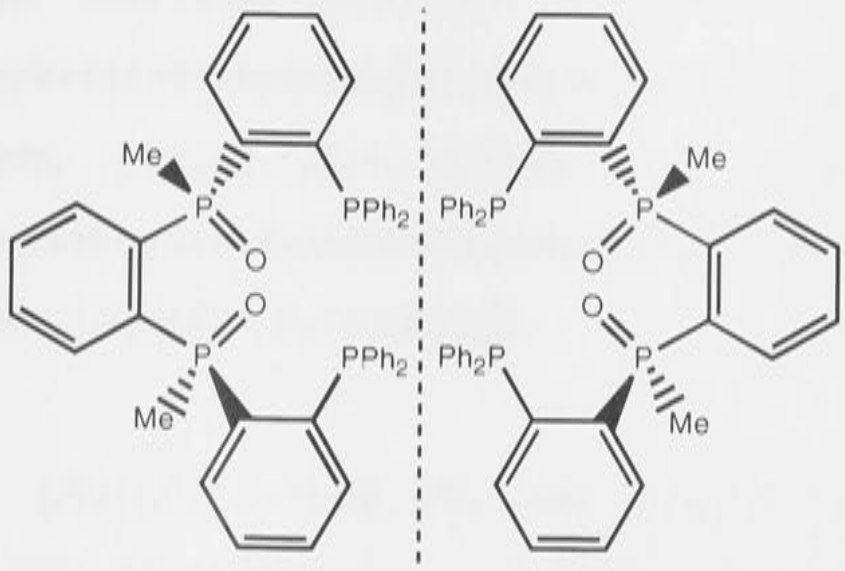
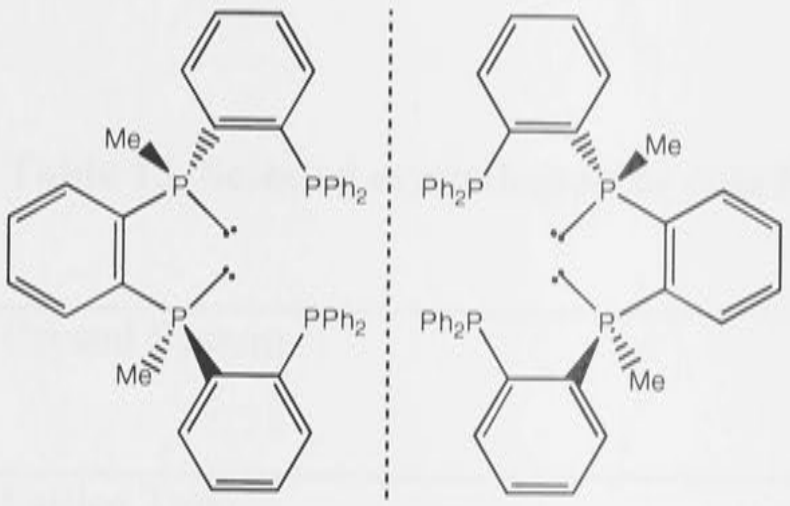


Figure 25 The dioxide (R_P*,R_P*)-1,2-bis[(2-diphenylphosphinophenyl)methylphosphinoyl]benzene [(R_P*,R_P*)-**58**‡].



(R_P*,R_P*)-**58**

(i) $[NBu_4][AuI_2]$/EtOH
(ii) NH_4PF_6/H_2O

$[Au\{(R_P*,R_P*)\text{-}\mathbf{58}\}]PF_6$

(i) $AgNO_3$/EtOH
(ii) NH_4PF_6/H_2O

$[Ag\{(R_P*,R_P*)\text{-}\mathbf{58}\}]PF_6$
+
$[Ag\{(R_P*,R_P*)\text{-}\mathbf{58}^{\ddagger}\}]PF_6$

Scheme 51

3.3.2 Crystal and Molecular Structures of [T-4-(R_P*,R_P*)]-(±)-{1,2-Bis[(2-diphenylphosphinophenyl)methylphosphino]benzene-P,P',P'',P'''}gold(I) Hexafluorophosphate, [Au{(R_P*,R_P*)-**58**}]PF_6, and [T-4-(R_P*,R_P*)]-(±)-{1,2-Bis[(2-diphenylphosphinophenyl)methylphosphinoyl]benzene-O,O',P,P'}silver(I) Hexafluorophosphate, [Ag{(R_P*,R_P*)-**58**‡}]PF_6

The structures of [Au{(R_P*,R_P*)-**58**}]PF_6 and [Ag{(R_P*,R_P*)-**58**‡}]PF_6 were determined by X-ray crystallography. Suitable crystals of the complex [Au{(R_P*,R_P*)-**58**}]PF_6 were obtained by slow diffusion of propan-2-ol into a solution of the complex in dichloromethane. The molecular structure of the cation [Au{(R_P*,R_P*)-**58**}]$^+$ is shown in Figure 26. Selected crystallographic data is shown in Tables 15 and 16. The molecular structure of the cation [Ag{(R_P*,R_P*)-**58**‡}]$^+$ is depicted in Figure 27, and selected crystallographic data in Tables 17 and 18.

Table 15 Selected crystallographic data for the complex [Au{(R_P*,R_P*)-**58**}]PF_6.

Crystal System	Triclinic
Lattice Type	Primitive
Space Group	$P\bar{1}$ (#2)
Lattice Parameters	a = 9.702(3) Å b = 14.545(4) Å c = 16.304(4) Å α = 86.957(2)° β = 76.013(2)° γ = 87.492(2)° V = 2228(1) Å^3

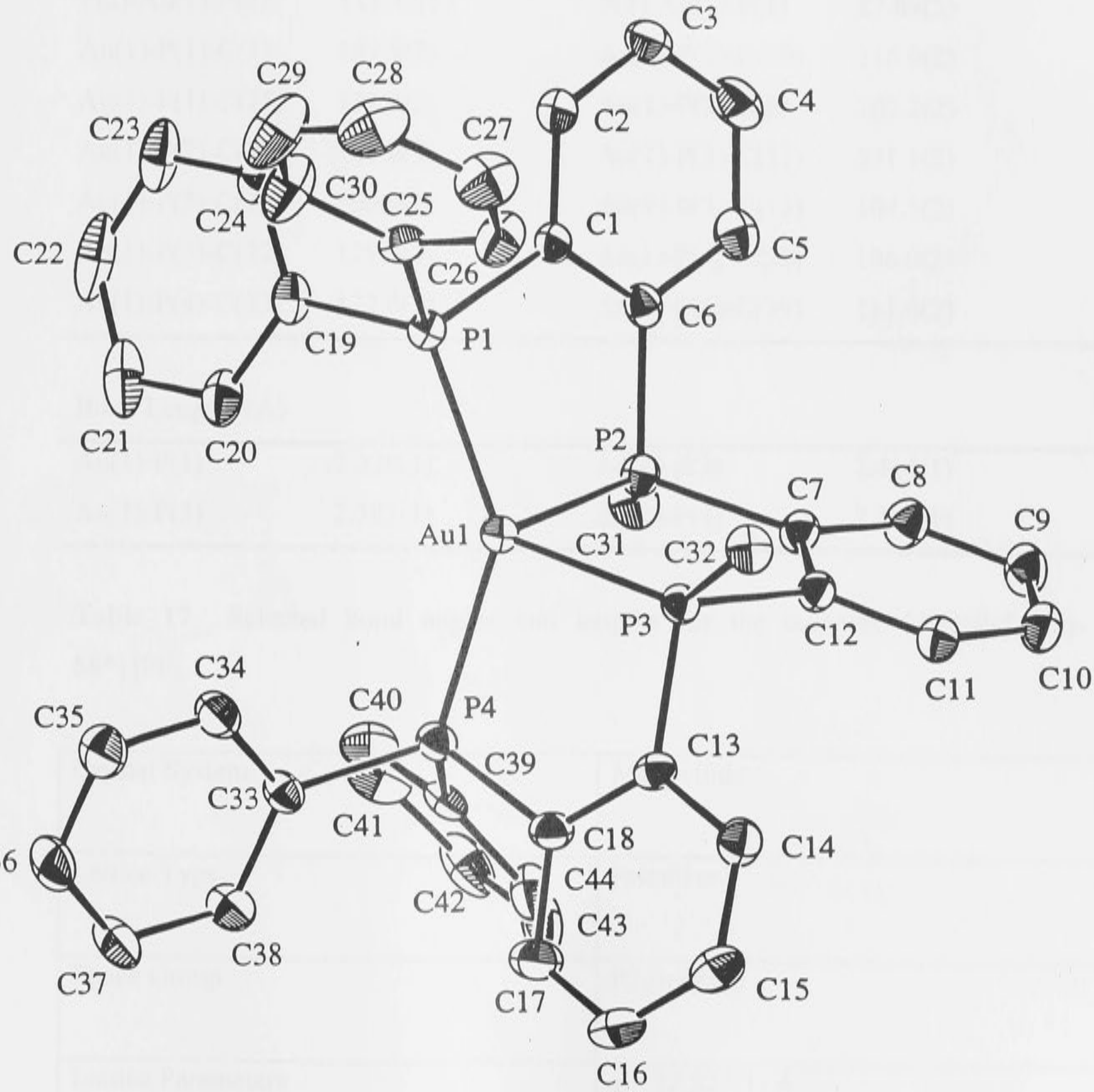


Figure 26 Molecular structure of the cation $[Au\{(R_P^*,R_P^*)\text{-}\mathbf{58}\}]^+$.

Table 16 Selected bond angles and lengths for the complex [Au{(R_P*,R_P*)-**58**}]PF_6.

Bond Angles (°)			
P(1)-Au(1)-P(2)	87.41(5)	P(1)-Au(1)-P(3)	124.82(5)
P(1)-Au(1)-P(4)	143.32(5)	P(2)-Au(1)-P(3)	86.22(5)
P(2)-Au(1)-P(4)	113.42(5)	P(3)-Au(1)-P(4)	87.89(5)
Au(1)-P(1)-C(1)	103.9(2)	Au(1)-P(1)-C(19)	116.0(2)
Au(1)-P(1)-C(25)	121.3(2)	Au(1)-P(2)-C(6)	102.2(2)
Au(1)-P(2)-C(7)	106.0(2)	Au(1)-P(2)-C(31)	131.1(2)
Au(1)-P(3)-C(12)	105.9(2)	Au(1)-P(3)-C(13)	104.5(2)
Au(1)-P(3)-C(32)	129.7(2)	Au(1)-P(4)-C(18)	106.0(2)
Au(1)-P(4)-C(33)	122.0(2)	Au(1)-P(4)-C(39)	111.6(2)

Bond Lengths (Å)			
Au(1)-P(1)	2.320(1)	Au(1)-P(2)	2.414(1)
Au(1)-P(3)	2.382(1)	Au(1)-P(4)	2.333(1)

Table 17 Selected bond angles and lengths for the complex [Ag{(R_P*,R_P*)-**58***}]PF_6.

Crystal System	Monoclinic
Lattice Type	Primitive
Space Group	$P2_1/n$ (#14)
Lattice Parameters	a = 12.220(1) Å b = 30.251(4) Å c = 13.932(2) Å α = 90° β = 102.059(1)° γ = 90°; V = 5036(1) $Å^3$

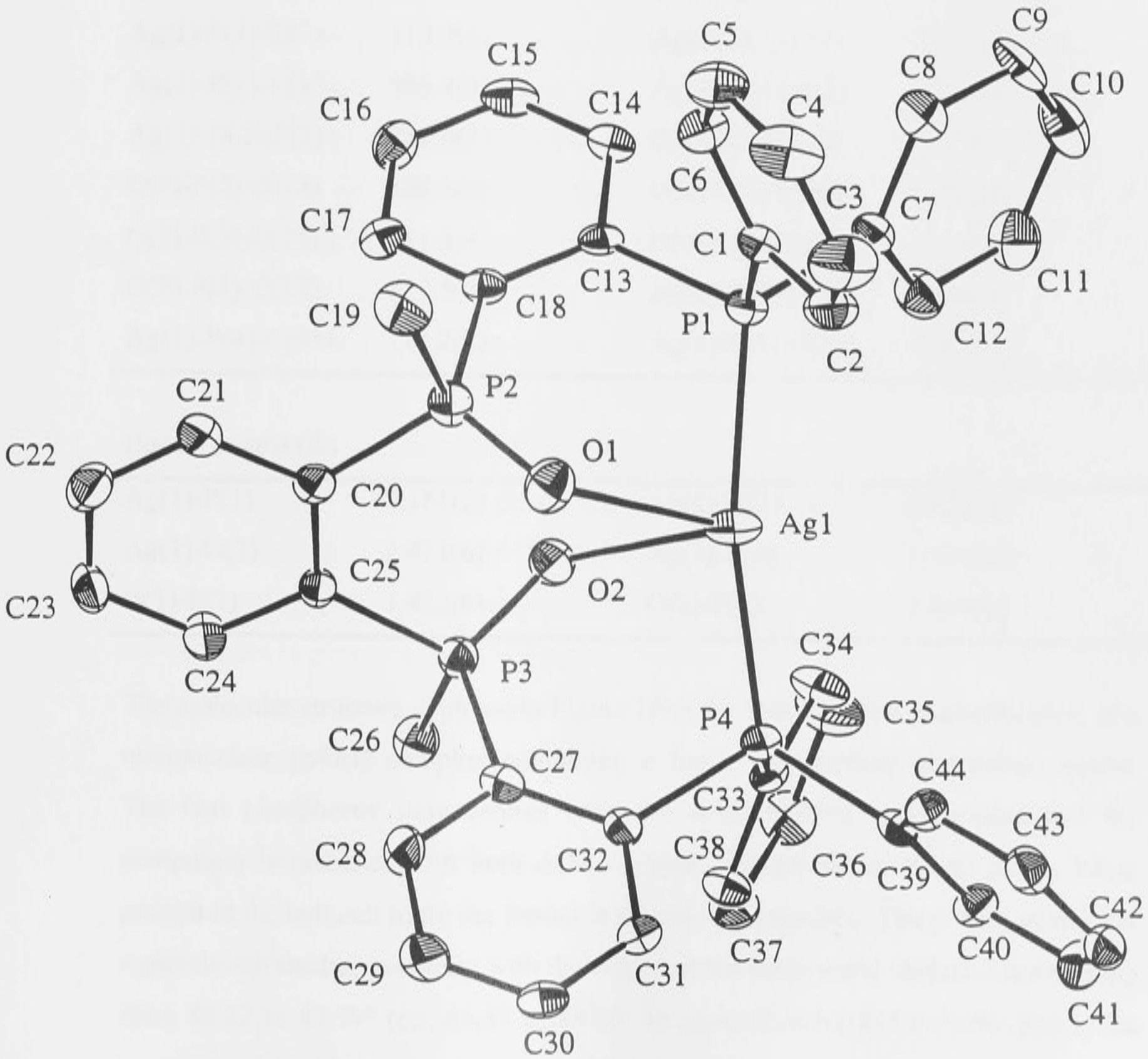


Figure 27 Molecular structure of the cation $[Ag\{(R_P^*,R_P^*)\text{-}\mathbf{58}^{\ddagger}\}]^+$.

Table 18 Selected bond angles and lengths for the complex [Ag{(R_P*,R_P*)-**58**‡}]PF_6.

Bond Angles (°)			
P(1)-Ag(1)-O(1)	87.41(5)	P(1)-Ag(1)-O(2)	103.3(1)
P(1)-Ag(1)-P(4)	166.86(8)	O(1)-Ag(1)-O(2)	74.0(2)
P(4)-Ag(1)-O(1)	111.4(2)	P(4)-Ag(1)-O(2)	80.4(1)
Ag(1)-P(1)-C(1)	113.9(3)	Ag(1)-P(1)-C(7)	118.0(3)
Ag(1)-P(1)-C(13)	108.4(3)	Ag(1)-O(1)-P(2)	122.8(3)
Ag(1)-O(2)-P(3)	122.4(3)	O(1)-P(2)-C(18)	118.1(4)
O(1)-P(2)-C(19)	108.1(4)	O(1)-P(2)-C(20)	114.1(4)
O(2)-P(3)-C(25)	111.4(4)	O(2)-P(3)-C(26)	111.4(4)
O(2)-P(3)-C(27)	117.5(4)	Ag(1)-P(4)-C(32)	110.0(3)
Ag(1)-P(4)-C(33)	111.2(2)	Ag(1)-P(4)-C(39)	120.4(3)

Bond Lengths (Å)			
Ag(1)-P(1)	2.381(2)	Ag(1)-O(1)	2.422(6)
Ag(1)-O(2)	2.471(6)	Ag(1)-P(4)	2.381(2)
O(1)-P(2)	1.452(6)	O(2)-P(3)	1.490(6)

The molecular structure depicted in Figure 26 is the first structural authentication of a mononuclear gold(I) complex containing a linear tetra(tertiary phosphine) ligand. The two phosphorus stereocentres have the same relative configuration and the compound is racemic, with both $\Delta(R_P,R_P)$ and $\Lambda(S_P,S_P)$ forms of the cation being present in the unit cell (only the former is shown in Figure 26). The gold(I) centre has a pseudo-tetrahedral geometry with the angles of the three metal chelate rings ranging from 86.22 to 87.79° (c.f. 86.39 to 89.16° in *cis*-α-[$CoCl_2$\{(R_P*,R_P*)-**58**\}]Cl). The presence of the three 1,2-phenylene linkages in the backbone of the tetra(tertiary phosphine) is the primary cause of the restrictive geometry about the metal centre and results in the rather large P(1)-Au(1)-P(4) angle of 143.32° (c.f 135.91° for the analogous P(1)-Cu(1)-P(4) bond angle in the related mononuclear, tetrahedral complex [Cu{(R_P,R_P)-tetraphos}]PF_6).[88]

The Au-P bond lengths for the internal phosphorus donor atoms (2.382 and 2.414 Å) are similar to the Au-P bond lengths in the bimetallic helicate $[Au_2\{(R_P,R_P)$-tetraphos)$\}](PF_6)_2$ which range between 2.38 - 2.44 Å.[88] It is noteworthy, however, that the bond distances associated with the terminal P donors and Au(I) (2.320 and 2.333 Å) are shorter, and hence stronger, than those between the internal P donors and the metal centre (2.382 and 2.414 Å), whereas the reverse trend was observed for *cis*-α-$[CoCl_2\{(R_P^*,R_P^*)$-**58**$\}]Cl$. This has an important implication in terms of oxygen insertion in these octahedral cobalt(III) and tetrahedral silver(I) complexes containing (R_P^*,R_P^*)-**58**, which in both instances appears to occur in the weaker metal-ligand bond. Insertion of an oxygen atom between a terminal phosphorus atom of **58** and cobalt(III) gave the complex *cis*-α-$[CoCl_2\{(R_P^*,R_P^*)$-**58***$\}]Cl$, whereas in the case of the related silver(I) complex, insertion of two oxygen atoms occurred between the two internal phosphorus atoms and the silver(I) centre to give $[Ag\{(R_P^*,R_P^*)$-**58**$^{\ddagger}\}]PF_6$.

The molecular structure depicted in Figure 27 clearly shows the presence of a mononuclear silver(I) cation containing a tetra(tertiary phosphine) dioxide. The complex can be envisioned as a [tetra(tertiary phosphine)]silver(I) complex in which oxygen atoms have been inserted between the internal phosphorus atoms and the metal centre to give two Ag-O-P bond sequences. The two phosphorus stereocentres have the same relative configuration with both $\Delta(R_P,R_P)$ and $\Lambda(S_P,S_P)$ forms of the cation being present in the unit cell. Only the latter is shown in Figure 27.

The silver(I) centre has a pseudo-tetrahedral geometry with angles about the metal centre of O(1)-Ag-O(2) 74.0°, P(1)-Ag-O(1) 87.41°, P(4)-Ag-O(1) 111.4°, P(1)-Ag-O(2) 103.3° and P(1)-Ag-P(4) 166.86°. The latter angle is significantly larger than that observed for $[Au\{(R_P^*,R_P^*)$-**58**$\}]PF_6$ and approaches the magnitude found in octahedral *cis*-α complexes containing linear tetra(tertiary phosphines). The Ag-P(1) and Ag-P(4) bond length of 2.381(2) Å is significantly shorter than Ag-P bond lengths previously reported for silver complexes containing di- and tetra-(tertiary phosphines). For example, the Ag-P bond length is 2.515 Å for the bis(bidentate) complex $[Ag(dppe)_2]NO_3$[133] and ranges between 2.48 - 2.54 Å for bimetallic helical complexes of the type $[Ag_2\{(R_P,R_P)$-tetraphos$\}_2](PF_6)_2$.[88]

3.3.3 $^{31}P\{^{1}H\}$ NMR Spectra of Tetrahedral Gold(I) and Silver(I) Complexes

The $^{31}P\{^{1}H\}$ NMR spectrum of the gold(I) complex [Au{(R_P*,R_P*)-**58**}]PF_6 in d_6-acetone can be rationalised in terms of its solid state structure. Two multiplets were observed at δ 3.7 and 23.6, which were assigned to the internal *P*Me and terminal *P*Ph_2 groups, respectively, on the basis that the ^{31}P resonances for triarylphosphino groups are typically found downfield from the analogous ^{31}P resonances for alkyldiarylphosphino groups in (tertiary phosphine)gold(I) complexes.[134] The spectral pattern observed for [Au{(R_P*,R_P*)-**58**}]PF_6 is consistent with that of a AXX'A' spin pattern (J_{AX} 131 Hz, $J_{A'X}$ 75 Hz, $J_{AA'}$ 41 Hz and $J_{XX'}$ 7 Hz). A similar pattern was observed in the $^{31}P\{^{1}H\}$ NMR spectrum of (R_P*,R_P*)-**58**.

The $^{31}P\{^{1}H\}$ NMR spectrum of [Ag{(R_P*,R_P*)-**58**‡}]PF_6 in d_2-dichloromethane exhibited a singlet at δ 46.2 and a pair of doublets centred at δ 13.1 [$^{1}J(^{107}Ag\text{-}^{31}P)$ -517 Hz and $^{1}J(^{109}Ag\text{-}^{31}P)$ -597 Hz] for the *P*(O)$MeAr_2$ groups and the *P*Ph_2 groups, respectively, consistent with the solid state structure. The sign of the coupling constants was assumed to be negative, by analogy with other silver(I) complexes containing tertiary phosphine ligands.[134,135]

The $^{31}P\{^{1}H\}$ NMR spectrum of [Ag{(R_P*,R_P*)-**58**}]PF_6, exhibited a sixteen line multiplet centred at δ 5.13 and an eight line multiplet centred at δ -33.0. The upfield resonance was assigned to the internal phosphorus stereocentres and the downfield resonance to the terminal phosphorus atoms of the co-ordinated ligand. The assignment was made on the basis that the chemical shift of the upfield signal was very similar to that observed for the stereogenic phosphorus atoms in (R_P*,R_P*)-**58**. Clearly the internal PMe groups of the ligand are at best only weakly co-ordinated to the silver(I) centre. In addition, no coupling of the stereogenic phosphorus atoms to the two isotopes of silver was observed at 25 °C. The terminal phosphorus centres, on the other hand, were coupled to both ^{107}Ag and ^{109}Ag [$^{1}J(^{107}Ag\text{-}^{31}P)$ -517 Hz, $^{1}J(^{109}Ag\text{-}^{31}P)$ -597 Hz].

3.4 SQUARE PLANAR COMPLEXES OF (R_P*,R_P*)-1,2-BIS[(2-DIPHENYLPHOSPHINOPHENYL)METHYLPHOSPHINO]BENZENE

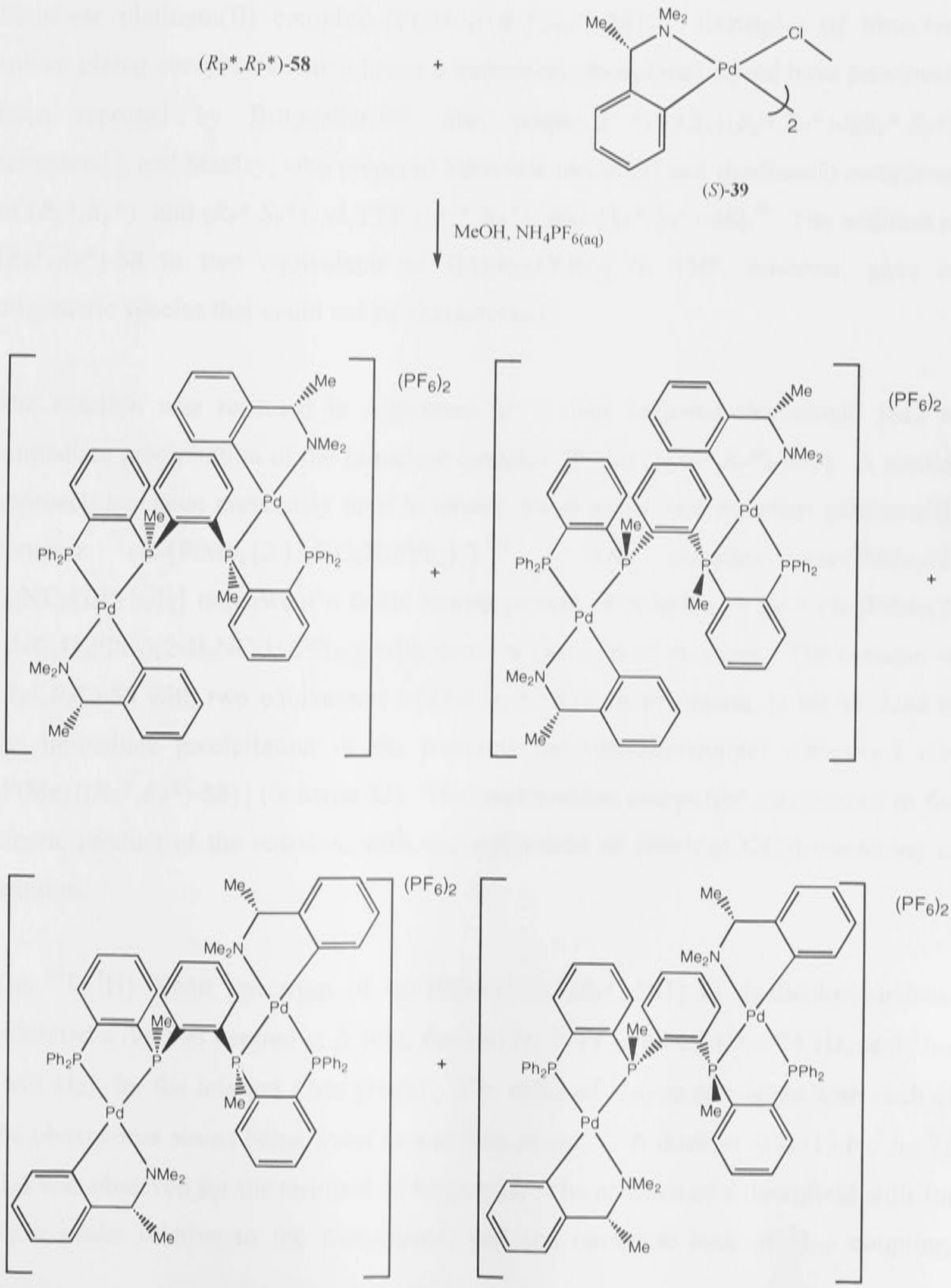
3.4.1 Attempted Resolution of (R_P*,R_P*)-1,2-Bis[(2-diphenylphosphinophenyl)-methylphosphino]benzene [(R_P*,R_P*)-58]

The only example of a racemic tetra(tertiary phosphine) to have been resolved by the method of metal complexation is (R_P*,R_P*)-tetraphos, *via* the separation by fractional crystallisation of a pair of diastereomeric binuclear palladium(II) salts derived from (*R*)-**39** (Section 1.3.5; Scheme 23).[87] A similar approach was utilised for the attempted resolution of (R_P*,R_P*)-**58**.

Reaction of equimolar amounts of the racemic ligand with (*S*)-**39** in methanol gave, upon the addition of aqueous ammonium hexafluorophosphate, a mixture of binuclear diastereomeric palladium(II) hexafluorophosphate salts (Scheme 52). The ^{1}H NMR spectrum of the mixture, in d_2-dichloromethane, was consistent with the presence of a maximum of four diastereomeric hexafluorophosphate salts. The structures shown in Scheme 52 assume that the two square planar units in each of the binuclear complexes have the same regiochemistry, as was observed in the resolution of tetraphos with (*R*)-**39**, and hence give rise to one set of NMR signals. This is not necessarily the case, as two sets of NMR signals would be observed if the regiochemistries of the two square planar units are different.

The spectrum revealed four doublets for the C*Me* groups at δ 1.16, 1.26, 1.33 and 1.46; four P*Me* resonances at δ 1.52, 1.69, 1.88 and 2.03; multiplet resonances for the N*Me* groups from δ 2.27 - 2.92; four methine resonances at δ 3.37, 3.60, 3.89 and 4.50; and multiplet aromatic resonances from δ 6.75 - 8.58. The combined non-aromatic to aromatic proton integration ratio was consistent with that for a binuclear complex containing one **58** ligand and two ortho-metalated (*S*)-dimethyl(1-phenylethyl)amine ligands. Furthermore, C, H, and N microanalysis of the

diastereomeric mixture was in agreement with the binuclear formulation, and FAB mass spectrometry exhibited a peak at m/e 1345, consistent with the presence of the binuclear cation $[Pd_2\{(S)\text{-}2\text{-}C_6H_4CH(Me)NMe_2\}_2\{\mu\text{-}(R_P{*},R_P{*})\textbf{-58}\}](PF_6)^+$. The diastereomeric complexes, however, could not be separated by fractional crystallisation.



Scheme 51

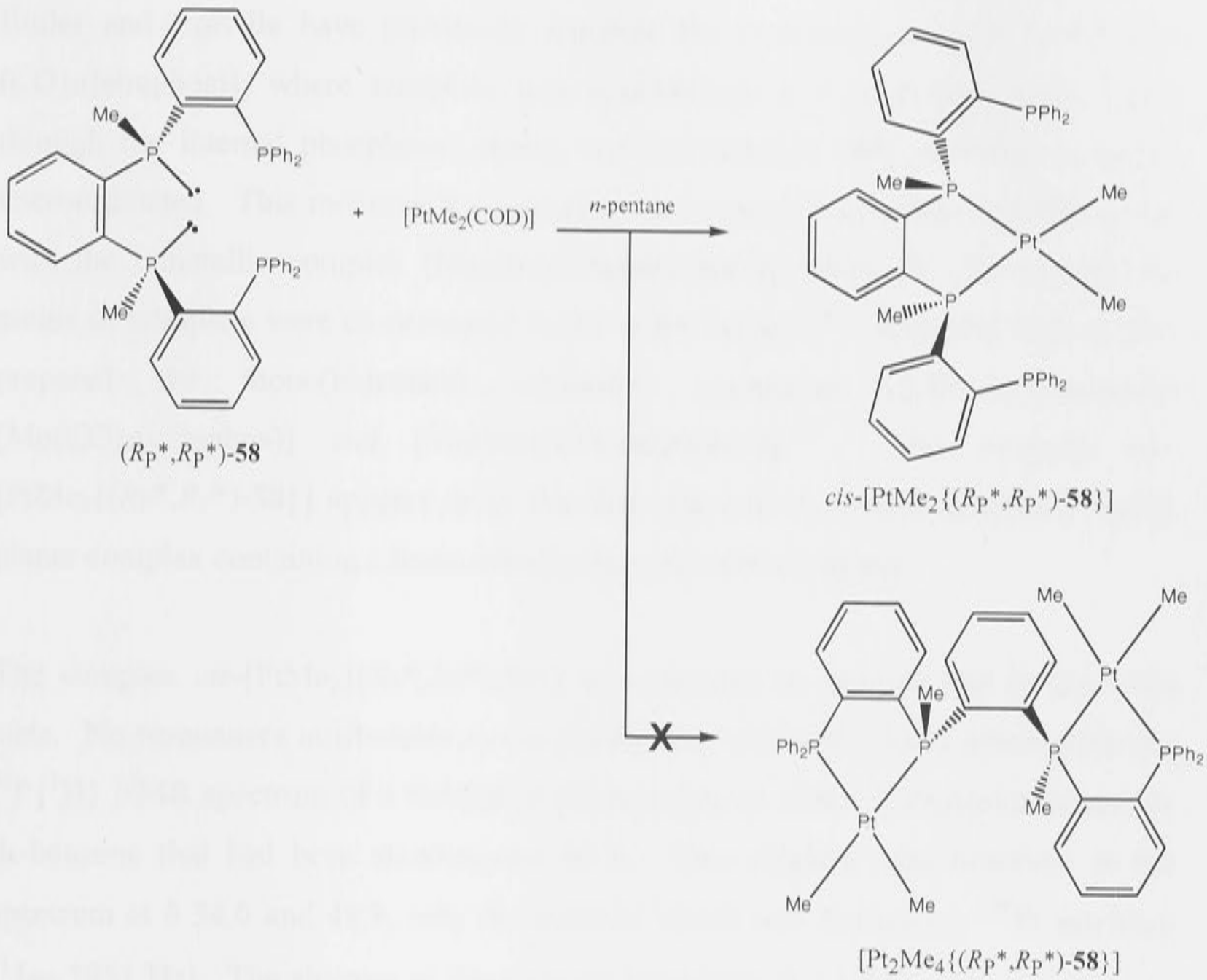
3.4.2 Platinum(II) Complexes of (R_P*,R_P*)-1,2-Bis[(2-diphenylphosphino-phenyl)methylphosphino]benzene [(R_P*,R_P*)-58]

The formation of binuclear palladium(II) complexes in the attempted resolution of (R_P*,R_P*)-**58** prompted an investigation into the co-ordination chemistry of (R_P*,R_P*)-**58** with platinum(II), in particular, the attempted preparation of the binuclear platinum(II) complex [Pt_2Me_4{(R_P*,R_P*)-**58**}]. Examples of binuclear square planar complexes with a linear tetra(tertiary phosphine) ligand have previously been reported by Brüggeller,[102] who prepared [Pt_2Cl_4{(R_P*,R_P*)-/(R_P*,S_P*)-tetraphos}], and Stanley, who prepared binuclear nickel(II) and rhodium(I) complexes of (R_P*,R_P*)- and (R_P*,S_P*)- eLTTP [(R_P*,R_P*)- and (R_P*,S_P*)-**46**].[89] The addition of (R_P*,R_P*)-**58** to two equivalents of [$PtMe_2$(COD)] in THF, however, gave an oligomeric species that could not be characterised.

The reaction was repeated in *n*-pentane, as it was believed this would lead to immediate precipitation of the binuclear complex [Pt_2Me_4{(R_P*,R_P*)-**58**}]. A similar approach has been previously used to isolate the mononuclear dimethyl platinum(II) complex *cis*-[$PtMe_2${2-$H_2NC_6H_4PPh_2$}$_2$].[136] The complex *cis*-[$PtMe_2${2-$H_2NC_6H_4PPh_2$}$_2$] underwent a facile rearrangement in solution to give *cis*-[PtMe(2-$HNC_6H_4PPh_2$)(2-$H_2NC_6H_4PPh_2$)] with concomitant loss of methane. The reaction of (R_P*,R_P*)-**58** with two equivalents of [$PtMe_2$(COD)] in *n*-pentane, however, lead to the immediate precipitation of the mononuclear mono(bidentate) compound *cis*-[$PtMe_2${(R_P*,R_P*)-**58**}] (Scheme 53). The mononuclear compound was formed as the kinetic product of the reaction, with one equivalent of [$PtMe_2$(COD)] remaining in solution.

The $^{31}P\{^1H\}$ NMR spectrum of *cis*-[$PtMe_2${(R_P*,R_P*)-**58**}] in d_2-dichloromethane exhibited a doublet centred at δ 30.0, flanked by ^{195}Pt satellites ($^2J_{PP}$ 75 Hz, and $^1J_{PtP}$ 1693 Hz), for the internal *P*Me groups. The value of $^1J_{PtP}$ is consistent with each of the phosphorus atoms being *trans* to a carbon atom.[137] A doublet at δ -13.0 ($^2J_{PP}$ 75 Hz) was observed for the terminal PPh_2 groups. The absence of a downfield shift for these peaks relative to the free ligand, and the complete lack of $^1J_{PtP}$ coupling,

indicated that the terminal PPh_2 groups were not coordinated to the platinum(II) centre.



$(R_P{*},R_P{*})$-**58**

cis-[$PtMe_2${$(R_P{*},R_P{*})$-**58**}]

[Pt_2Me_4{$(R_P{*},R_P{*})$-**58**}]

(only one enantiomer of each chiral species is shown)

Scheme 53

The ^1H NMR spectrum of *cis*-[$PtMe_2${$(R_P{*},R_P{*})$-**58**}] in the same solvent, revealed a broad doublet at δ 2.10 attributable to the P*Me* groups. The resonance was flanked by platinum satellites, due to both ^{195}Pt and ^{31}P coupling to the methyl protons ($^2J_{PH}$ 4.92 Hz, $^3J_{PtH}$ 46.7 Hz). The Pt*Me* resonance was observed at δ 0.15, as a complex pattern that was not susceptible to first order analysis. It was an example of an $AA'MX_3X'_3$ splitting pattern, which has been previously observed for square planar complexes of the type *cis*-[$PtMe_2(PR_3)_2$].[138,139] The upfield shift of the Pt*Me* resonance was a consequence of shielding by the phenyl groups of the terminal phosphorus atoms of the tetradentate ligand. The integration ratio of aromatic to methyl protons was consistent with that of the mononuclear complex.

There are a number of examples of octahedral complexes containing a linear tetra(tertiary phosphine) co-ordinated through the internal phosphorus atoms only. Butler and Colville have previously reported the octahedral complex *fac*-[$MnBr(CO)_3$(tetraphos)], where tetraphos was coordinated as a mono(bidentate) ligand through the internal phosphorus atoms, and the terminal PPh_2 moieties remained unco-ordinated. This mononuclear complex was a co-product of the reaction, along with the bimetallic complex [$Mn_2Br_2(CO)_6$(tetraphos)] where all four phosphorus atoms of tetraphos were co-ordinated to the metal centres.[140] King and Kapoor also prepared the mono(bidentate) octahedral complexes [$Cr(CO)_4$(tetraphos)], [$Mo(CO)_4$(tetraphos)] and [$Mn(Me)(CO)_4$(tetraphos)].[141] The complex *cis*-[$PtMe_2$\{(R_P*,R_P*)-**58**\}] appears to be the first example of a mono(bidentate) square planar complex containing a linear tetra(tertiary phosphine) ligand.

The complex *cis*-[$PtMe_2$\{(R_P*,R_P*)-**58**\}] was unstable in solution and in the solid state. No resonances attributable to *cis*-[$PtMe_2$\{(R_P*,R_P*)-**58**\}] were observed in the $^{31}P\{^1H\}$ NMR spectrum of a sample of the complex in either d_2-dichloromethane or d_6-benzene that had been standing for 48 h. Two singlets were observed in the spectrum at δ 34.0 and 48.9, only the latter of which was flanked by ^{195}Pt satellites ($^1J_{PtP}$ 1851 Hz). The absence of the peaks in the region δ -11.9 to -14.0 is consistent with oxidation of the terminal diphenylphosphino groups in *cis*-[$PtMe_2$\{(R_P*,R_P*)-**58**\}].

Chapter Four

Conclusion

4.1 CONCLUSION

This thesis details the first stereoselective syntheses of chiral linear tetra(tertiary phosphines). Three ligands of this type have been prepared by two synthetic routes: *via* the reaction of a 2-chlorophenyl substituted di(tertiary phosphine) with sodium (2-dimethylphosphinophenyl)methylphosphide or by the reaction of two equivalents of a 2-chlorophenyl substituted tertiary phosphine with sodium 1,2-phenylenebis-(dimethylphosphide). The incorporation of three rigid 1,2-phenylene groups into the ligand backbone is believed to be responsible for the high stereoselectivity observed in this work. The linear tetra(tertiary phosphines) (R_P*,R_P*)-1,2-bis[(2-dimethylphosphinophenyl)methylphosphino]benzene [(R_P*,R_P*)-**57**], (R_P*,R_P*)-1,2-bis[(2-diphenylphosphinophenyl)methylphosphino]benzene [(R_P*,R_P*)-**58**] were prepared in a completely stereoselective manner, and (R_P*,R_P*,R_P*,S_P*)-1,2-bis[(2-methylphenylphosphinophenyl)methylphosphino]benzene [(R_P*,R_P*,R_P*,S_P*)-**59**] was prepared with 90% stereoselectivity. The latter is the first example of a linear tetra(tertiary phosphine) containing four stereogenic phosphorus stereocentres.

Moreover, all three ligands formed the *cis*-α diastereomer exclusively on co-ordination to cobalt(III). Optically active tetra(tertiary phosphines) that form *cis*-α complexes offer enormous potential as chiral auxiliaries in asymmetric synthesis and catalysis, particularly in controlling the stereoselectivity of reactions involving substrates that bind in a bidentate fashion.

There are, however, very few reports of linear tetra(tertiary phosphines) having been used in catalysis. Suarez and Fontal have reported the complex *trans*-[$RuCl_2${(R_P*,S_P*)-tetraphos}] to be an efficient catalyst for the hydrogenation, and hydroformylation, of ethylene and 1-hexene. Indeed, the complex proved to be an equally effective, if not moreso, catalyst as analogous ruthenium(II) complexes containing the tripodal tetra(tertiary phosphine) **20** and the tripodal tri(tertiary phosphines) $C(CH_2PPh_2)_3$ and $N(CH_2CH_2PPh_2)_3$ in these reactions.[142] Stanley and co-workers have reported similar results for binuclear Rh(I) complexes containing the ligand (R_P*,R_P*)- or (R_P*,S_P*)-eLTTP [(R_P*,R_P*)- or (R_P*,S_P*)-**46**].[91] Furthermore,

the analogous rhodium(I) complexes containing the optically active antipodes of the ligand proved effective as chiral auxiliaries in the asymmetric hydroformylation of a number of vinyl ester substrates, with enantioselectivities as high as 85% (section 1.3.2.4).[90]

Despite these encouraging results, the role of linear tetra(tertiary phosphines) as chiral auxiliaries in enantioselective catalysis has remained largely unexplored. This is undoubtedly due, in part, to the fact that synthetic routes to compounds of this type are often tedious, low yielding and invariably result in the generation of two or more diastereomeric forms of the ligand. Consequently, separation of the diastereomers, followed by resolution of the racemic diastereomer is typically required to give the optically pure antipodes of the tetra(tertiary phosphine). The prospect is particularly daunting when the ligand contains four stereogenic phosphorus centres, as a tetra(tertiary phosphine) of this type has six possible diastereomeric forms. Furthermore, the tetra(tertiary phosphine) may not necessarily form a single diastereomeric complex upon co-ordination to an octahedral metal ion. A feature of the syntheses detailed in this work is that both the ligands, and their transition metal complexes, were synthesised in a highly stereoselective manner.

The synthesis of optically active analogues of the linear tetra(tertiary phosphines) can be envisaged in two ways. Firstly, by the use of an optically active 2-chlorophenyl substituted tertiary or di(tertiary phosphine) or secondly, *via* the resolution of the racemic tetra(tertiary phosphine). Both approaches have been investigated in this work. The asymmetric di(tertiary phosphine) (±)-(2-chlorophenyl)(2-dimethylphosphinophenyl)-methylphosphine [(±)-**56**] [the precursor to (R_P*,R_P*)-**57**], was successfully resolved by the method of metal complexation. The reaction of the racemic ligand [(±)-**56**] with the resolving agent di-μ-chlorobis{(*S*)-[1-(dimethylamino)ethyl]naphthyl-C^2N}dipalladium-(II) [(*S*)-**72**] in methanol, followed by the addition of aqueous ammonium hexafluorophosphate, gave a separable mixture of four diastereomeric palladium(II) complexes. Two of these diastereomeric palladium(II) complexes were isolated in a diastereomerically pure form by fractional crystallisation, albeit in low yields. Subsequent decomplexation gave small quantities of the optically active antipodes of the di(tertiary phosphine).

A similar approach could be used for the resolution of (±)-(2-chlorophenyl)methylphenylphosphine [the precursor to **59**]. However, this has not been investigated in the current work. A number of racemic monodentate tertiary phosphines have been resolved *via* the method of metal complexation.[119,143,144]

Resolution of the tetra(tertiary phosphine) (R_P*,R_P*)-**58** by the method of metal complexation has been investigated during the course of the work. The reaction of (R_P*,R_P*)-**58** with di-μ-chloro-bis{(*S*)-2-[1-(dimethylamino)ethyl]phenyl-C^1,N}di-palladium(II) [(*S*)-**39**], or (*S*)-**72**, gave a mixture of diastereomeric palladium(II) salts that could not be separated by fractional crystallisation from a range of solvent systems. The resolution of (R_P*,R_P*)-**58** by fractional crystallisation of a pair of diastereomeric cobalt(III) D-(-)-dibenzoyl hydrogen tartrate salts containing the ligand was also investigated but again no separation of the diastereomers was observed. The neutral ruthenium(II) complex *cis*-α-[$RuCl_2${(R_P*,R_P*)-**58**}] was also prepared in this work. Substitution of a chloro group of *cis*-α-[$RuCl_2${(R_P*,R_P*)-**58**}] by an optically active amine, followed by separation of the diastereomers, could provide a means of resolution of (R_P*,R_P*)-**58**. Furthermore, the optically active ruthenium(II) complex *cis*-α-[$RuCl_2${(R_P,R_P)-**58**}] (or its enantiomer) is an excellent candidate as a catalyst in the asymmetric hydrogenation and hydroformylation of alkenes.

The gold(I) complex [Au{(R_P*,R_P*)-**58**}]PF_6 was also prepared and its structure determined by X-ray analysis. It is the first example of a mononuclear gold(I) complex containing a linear tetra(tertiary phosphine) to have been structurally authenticated. The formation of a mononuclear complex, as opposed to a binuclear complex, can be rationalised by the presence of three 1,2-phenylene linkages in the ligand backbone, which preclude formation of anything but a mononuclear complex. The complex is of great interest as a potential anticancer agent. (Tertiary phosphine)gold(I) complexes, in general, have been found to rapidly accumulate in mitochondria by virtue of their lipophilic, cationic nature, and to inhibit the activity of ATP synthase leading to rapid cell death. The complex [Au{(R_P*,R_P*)-**58**}]PF_6 was found to exhibit potent *in vitro* cytotoxicity against the mouse tumour cell line P388 leukaemia. Furthermore, the complex and [Au{(R_P*,R_P*)-tetraphos}$_2$]$(PF_6)_2$ have

been shown to selectivity target mitochondria with relatively high mitochondrial membrane potentials.[111] The greater kinetic inertness of [tetra(tertiary phosphine)]gold(I) complexes relative to their bis[di(tertiary phosphine)]gold(I) counterparts appears to be the key to their modified cytotoxic activity.

Chapter Five

Experimental

5.1 GENERAL

Reactions involving air-sensitive compounds were performed under a positive pressure of argon using Schlenk techniques. All solvents were deoxygenated prior to use. Benzene, diethyl ether and tetrahydrofuran were dried over sodium and distilled using benzophenone ketyl as indicator. 1,2-Dichlorobenzene was dried over calcium hydride, distilled under vacuum, and stored under argon over molecular sieves, prior to use. Trimethylchlorosilane was distilled under argon not more than 24 h prior to use. All other reagents were of analytical grade and used without further purificaton.

NMR spectra were obtained using a Varian Gemini 300 spectrometer operating at 300 MHz (^{1}H) and 121.5 MHz [$^{31}P\{^{1}H\}$]. All chemical shift values (δ) are reported in ppm. ^{1}H NMR chemical shift values are relative to tetramethylsilane and $^{31}P\{^{1}H\}$ NMR chemical shift values are referenced relative to external 85% aqueous H_3PO_4. GC/MS spectra were recorded on a Hewlett Packard G1800A spectrometer. Mass spectra for compounds with molecular weights over 400 were obtained on a VG Micromass (70 eV) spectrometer.

All elemental analyses were carried out by staff within the micro-analytical laboratory at the Research School of Chemistry.

The optically active palladium(II) resolving agent di-μ-chlorobis{(S)-[1-(dimethylamino)ethyl]naphthyl-C^2N}dipalladium(II) was obtained from Mr Paul Gugger, Research School of Chemistry. Methylphenylphosphine was prepared by Dr Roy Doyle, dichlorotetrakis(dimethylsulfoxide)ruthenium(II) was prepared by Dr Mark Lynch, tetrabutylammonium diiodoaurate was prepared by Mr Peter Papathanasiou, and (1,5-cyclooctadiene)diiodoplatinum(II) was prepared by Ms Natalie Ward.

5.2 SYNTHETIC PROCEDURES

5.2.1 Synthesis of Tetramethyl 1,2-Phenylenebis(phosphonate) (62)

The di(phosphonate) tetramethyl 1,2-phenylenebis(phosphonate) (**62**) was prepared by a modified literature procedure.[114]

A 3:1 mixture of trimethyl phosphite (758 g, 6.11 mol) and 1,2-dichlorobenzene (299 g, 2.04 mol) was photolysed at 80 °C using a 400 W mercury medium pressure vapour lamp, for 5 days. The reaction mixture was kept under nitrogen. After this time, the unreacted starting materials were distilled off under reduced pressure. The resulting oil was left at -5 °C overnight, whereupon it became a solid mass. Acetone (200 mL) was cooled to -15 °C and added to the solid. The white solid was filtered and washed with diethyl ether (30 mL). Acetone (150 mL) was added to the filtrate and the solution was left at -5 °C overnight to give a further crop of crystals. The remaining filtrate contained the mono-substituted product dimethyl (2-chlorophenyl)phosphonate (**63**), which could be recycled, with the recovered trimethyl phosphite and 1,2-dichlorobenzene, in the photolysis reaction. The combined product was dried under vacuum (0.1 mmHg) for 48 h. M.p 80.5 - 81 °C (lit.[114] 79 - 81 °C). Yield 328 g (41%). Anal. calcd for $C_{10}H_{16}O_6P_2$: C, 40.83; H, 5.48. Found: C, 40.51; H, 5.32. ^{1}H NMR (d_1-chloroform): δ 3.84 (d of d, 12 H, $^3J_{PH}$ 11.25 Hz, $^6J_{P'H}$ 0.78 Hz, PO*Me*), 7.64 - 8.18 (m, 4 H, *aromatics*). $^{31}P\{^1H\}$ NMR (d_1-chloroform): δ -19.2 (s, 2 P). m/e 294 $(M)^+$, 279 $(M\text{-}Me)^+$, 263 $(M\text{-}OMe)^+$, 185 $[M\text{-}P(O)(OMe)_2]^+$.

5.2.2 Synthesis of 1,2-Phenylenebis(phosphine) (64)

The bis(primary phosphine) 1,2-phenylenebis(phosphine) (**64**) was prepared by a modified literature procedure.[114]

Lithium aluminium hydride (31.70 g, 0.835 mol) was added to THF (300 mL) at -78 °C, and to this suspension chlorotrimethylsilane (90.71 g, 0.835 mol) was added dropwise. The light grey suspension was allowed to warm to room temperature and stirred for a further 2.5 h. The mixture was then cooled to -30 °C and a solution of tetramethyl 1,2-phenylenebis(phosphonate), **62**, (40.26 g, 0.137 mol) in THF (120 mL) was added dropwise. The reaction mixture was stirred for 48 h.

Water (1 mL/g $LiAlH_4$) was added cautiously to the mixture, followed by aqueous NaOH (15% (w/v), 1 mL/g $LiAlH_4$). Further water (200 mL) was added slowly, until a white precipitate settled at the bottom of the flask. The precipitate was allowed to settle over 2 h. The solution was decanted off, and the precipitate was washed with THF (2 x 200 mL).

The solvent of the combined filtrate was removed by distillation under argon, and diethyl ether (200 mL) was added to the residue. The solution was dried ($MgSO_4$), filtered, and the solvent removed to give a yellow oil. The product was obtained as a colourless oil by vacuum distillation. B.p 52 °C (0.02 mmHg) [lit.[114] 53 - 55 °C (0.25 mmHg)]. Yield 14.12 g (73%). ^{1}H NMR (d_6-benzene): δ 3.84 (d of m, 4 H, $^1J_{PH}$ 207 Hz, P*H*$_2$), 6.82 - 7.24 (m, 4 H, *aromatics*). $^{31}P\{^1H\}$ NMR (d_6-benzene): δ -124.8 (s, 2 P). m/e: 142 $(M)^+$, 109 $(M\text{-}PH_2)^+$.

5.2.3 Synthesis of (R_P*,R_P*)- and (R_P*,S_P*)-1,2-Phenylenebis(methylphosphine) [(R_P*,R_P*)- and (R_P*,S_P*)-65]

The bis(secondary phosphine) (R_P*,R_P*)- and (R_P*,S_P*)-1,2-phenylenebis(methylphosphine) [(R_P*,R_P*)- and (R_P*,S_P*)-**65**] was prepared by two different methods.

Method 1 (based on a modified literature procedure[114])

n-Butyllithium (1.39 M, 61.39 mL, 0.085 mol) was added dropwise to a solution of 1,2-phenylenebis(phosphine), **64**, (6.06 g, 0.043 mol) in THF (60 mL) at -78 °C, and the solution was stirred for 30 mins. A solution of methyl iodide (12.11 g, 0.042 mol) in THF (40 mL) was added dropwise, and the reaction mixture was stirred overnight. The solvent was then removed, and water (100 mL), and diethyl ether (80 mL) was added to the residue. The phases were separated, and the aqueous layer was extracted with diethyl ether (2 x 80 mL). The diethyl ether extracts were dried ($MgSO_4$), filtered and the solvent was removed to give a yellow oil. The product was obtained as a colourless oil by vacuum distillation. B.p 64 - 65 °C (0.02 mmHg). [lit.[114] 69 - 70 °C (0.3 mmHg)]. Yield 5.64 g (78%). The product was isolated as a *ca* 1:1 mixture of racemic and meso diastereomers, and also contained between 5-20% of (±)-(2-dimethylphosphinophenyl)methylphosphine [(±)-**66**] and could not be further purified by fractional distillation.

Method 2

Sodium foil (4.30 g, 0.187 mol) was added piecewise to a solution of 1,2-phenylenebis(phosphine), **64**, (14.12 g, 0.099 mol) in THF (200 mL), and the reaction mixture was allowed to stir for 48 h. Any excess sodium was removed, and the orange solution was cooled to -78 °C. Methyl iodide (11.64 g, 0.187 mol) in THF (20 mL) was added dropwise, and the solution was stirred overnight. The solvent was distilled off under argon. Water (100 mL) was added to the residue, and the aqueous phase was extracted with diethyl ether (3 x 100 mL). The combined diethyl ether extracts were dried ($MgSO_4$), filtered and the solvent distilled off under argon, leaving

a yellow oil. The product was obtained as a colourless oil by vacuum distillation. B.p 58 - 60 °C (0.001 mmHg). Yield 14.16 g (84%). The product was isolated as a *ca* 1:1 mixture of racemic and meso diastereomers and also contained *ca* 5% of (±)-(2-methylphosphinophenyl)phosphine [(±)-**67**], and could not be further purified by fractional distillation. ^{1}H NMR (d_6-benzene): δ 1.13 (d of t, 6 H, $^{3}J_{HH}$ 7.14 Hz, $|^{2}J_{PH} + {}^{5}J_{P'H}|$ 3.60 Hz, P*Me*), 1.16 (d of t, 6 H, $^{3}J_{HH}$ 7.41 Hz, $|^{2}J_{PH} + {}^{5}J_{P'H}|$ 3.30 Hz, P*Me*), 4.23 (d of q, 2 H, $^{2}J_{PH}$ 216.4 Hz, $^{3}J_{HH}$ 7.14 Hz, P*H*), 4.37 (d of q, 2 H, $^{2}J_{PH}$ 213.4 Hz, $^{3}J_{HH}$ 7.41 Hz, P*H*), 6.99 - 7.28 (m, 8 H, *aromatics*). ^{31}P{^{1}H} NMR (d_6-benzene): δ -73.6 (s, 2 P), -74.7 (s, 2 P). m/e: 170 $(M)^+$, 155 $(M\text{-}Me)^+$, 123 $(M\text{-}PHMe)^+$.

5.2.4 Synthesis of (±)-(2-Dimethylphosphinophenyl)methylphosphine [(±)-66]

The secondary phosphine (±)-(2-dimethylphosphinophenyl)methylphosphine [(±)-**66**] was prepared by three different methods.

Method 1

n-Butyllithium (1.44 M, 19.89 mL, 0.029 mol) was added dropwise to a solution of (R_P*,R_P*)- and (R_P*,S_P*)-1,2-phenylenebis(methylphosphine), (R_P*,R_P*)- and (R_P*,S_P*)-**65**, (4.87 g, 0.029 mol) in THF (50 mL) at -78 °C. The solution was stirred for an hour, and a solution of methyl iodide (4.07 g, 0.029 mol) in THF (30 mL) was added dropwise. The solution was warmed to room temperature and stirred overnight. The solvents were then removed under vacuum. Water (80 mL) was added to the residue, and the aqueous phase was extracted with diethyl ether (3 x 80 mL). The diethyl ether extracts were dried ($MgSO_4$), filtered and the ether was removed under vacuum to leave a yellow oil. Vacuum distillation of the oil gave the product as a colourless oil. B.p 64 °C (0.004 mmHg). Yield 4.47 g (85%). The product contained *ca* 10% of the bis (secondary phosphine) (R_P*,R_P*)- and (R_P*,S_P*)- 1,2-phenylenebis(methylphosphine) [(R_P*,R_P*)- and (R_P*,S_P*)-**65**] and 15% of 1,2-phenylenebis(dimethylphosphine) (**68**).

Method 2

Sodium foil (0.58 g, 0.025 mol) was added to a solution of (R_P*,R_P*)- and (R_P*,S_P*)-1,2-phenylenebis(methylphosphine), (R_P*,R_P*)- and (R_P*,S_P*)-**65**, (4.28 g, 0.025 mol) in THF (50 mL) at -78 °C. The reaction mixture was allowed to warm to room temperature and was stirred overnight. The deep red solution was cooled to -78 °C, and a solution of methyl iodide (3.57 g, 0.025 mol) in THF (30 mL) was added dropwise. The reaction mixture was allowed to warm to room temperature and was stirred overnight. The solvent was removed, and water (50 mL) was added to the residue. The aqueous phase was extracted with diethyl ether (3 x 60 mL). The diethyl ether extracts were dried ($MgSO_4$), filtered, and the solvent removed to leave a yellow oil. Vacuum distillation of the yellow oil gave the product as a colourless oil. B.p 65 °C (0.004 mmHg). Yield 3.56 g (77%). The product contained 17% of (R_P*,R_P*)- and (R_P*,S_P*)-1,2-phenylenebis(methylphosphine) [(R_P*,R_P*)- and (R_P*,S_P*)-**65**] and 18% of 1,2-phenylenebis(dimethylphosphine) (**68**).

Method 3

Liquid ammonia (200 mL) was condensed onto (R_P*,R_P*)- and (R_P*,S_P*)-1,2-phenylenebis(methylphosphine), (R_P*,R_P*)- and (R_P*,S_P*)-**65**, (14.16 g, 0.083 mol). An excess of potassium metal pieces (4.01 g, 0.102 mol) was added to the solution and the reaction mixture was stirred for 4 h. A solution of methyl iodide (14.54 g, 0.102 mol) in THF (25 mL) was added dropwise. The colourless solution was allowed to warm to room temperature overnight. Water (100 mL) was added to the residue, and the aqueous phase was extracted with diethyl ether (3 x 100 mL). The diethyl ether extracts were dried ($MgSO_4$), filtered and the solvent distilled off under argon, leaving a yellow oil. Vacuum distillation of the crude oil gave the product as a colourless oil. B.p 67 - 68 °C (0.005 mmHg). Yield 14.11 g (92%). The product contained 4% of (R_P*,R_P*)- and (R_P*,S_P*)-1,2-phenylenebis(methylphosphine) [(R_P*,R_P*)- and (R_P*,S_P*)-**65**] and 22% of 1,2-phenylenebis(dimethylphosphine) (**68**). ^{1}H NMR (d_6-benzene): δ 1.08 (d, 3 H, $^2J_{PH}$ 3.99 Hz, P*Me*Me), 1.13 (d, 3 H, $^2J_{PH}$ 3.42 Hz, PMe*Me*), 1.27 (d of d of d, 3 H, $^3J_{HH}$ 7.41 Hz, $^2J_{PH}$ 3.58 Hz, $^5J_{P'H}$ 0.63 Hz, PH*Me*), 4.45 (d of d of q, 1 H, $^1J_{PH}$ 208.7 Hz, $^4J_{P'H}$ 11.01 Hz, $^3J_{PHH}$ 7.41 Hz, P*H*), 6.98 - 7.36

(m, 4 H, *aromatics*). ^{31}P $\{^{1}H\}$ NMR (d_6-benzene): δ -72.5 (d, 1 P, $^{3}J_{PP}$ 122 Hz, *P*HMe), -54.4 (d, 1 P, $^{3}J_{PP}$ 122 Hz *P*Me_2). m/e: 184 $(M)^+$, 169 $(M\text{-}Me)^+$, 123 $(M\text{-}PMe_2)^+$.

5.2.5 Synthesis of 1,2-Phenylenebis(dimethylphosphine) (68)

Excess sodium foil (3.04 g, 0.132 mol) was added to (R_P*,R_P*)- and (R_P*,S_P*)-1,2-phenylenebis(methylphosphine), (R_P*,R_P*)- and (R_P*,S_P*)-**65**, (7.56 g, 0.044 mol) in THF (120 mL), and the solution was stirred overnight. The excess sodium was removed, and the orange solution was cooled to -78 °C. A solution of methyl iodide (12.61 g, 0.089 mol) in THF (30 mL) was added dropwise. The solution was allowed to come to room temperature and was stirred overnight. The solvent was removed, water (80 mL) was added to the residue, and the aqueous phase was extracted with diethyl ether (3 x 80 mL). The combined ether extracts were dried ($MgSO_4$), filtered, and the solvent removed to leave a yellow oil. Vacuum distillation of the crude oil gave the product as a colourless oil. B.p 78 °C (0.001 mmHg) [lit.[114] 139 - 141 °C (0.4 - 0.5 mmHg)]. Yield 7.10 g (81%). ^{1}H NMR (d_6-benzene): δ 1.22 (t, 12 H, $^{2}J_{PH}$ 1.73 Hz, P*Me*$_2$), 7.1 - 7.35 (m, 4 H, *aromatics*). $^{31}P\{^{1}H\}$ NMR (d_6-benzene): δ -54.8 (s, 2 P, *P*Me_2). m/e: 198 $(M)^+$ 183 $(M\text{-}Me)^+$

5.2.6 Reaction Between 1,2-Phenylenebis(dimethylphosphine) and Sodium in Liquid Ammonia

Liquid ammonia (200 mL) was condensed onto 1,2-phenylenebis-(dimethylphosphine), **68**, (7.08 g, 0.035 mol) at -78 °C. Sodium foil (0.82 g, 0.035 mol) was added piecewise, and the resulting dark red solution was stirred for two hours. An aliquot was taken, quenched with water, and the solvent removed. The GC-MS showed the major product to be dimethylphenylphosphine, [m/e 138 $(M)^+$, 123 $(M\text{-}Me)^+$] consistent with cleavage of a single dimethylphosphino group from

1,2-phenylenebis(dimethylphosphine). A small amount of (±)-(2-dimethylphosphino)methylphosphine [(±)-**66**] (*ca* 3%) was identified in the reaction products.

5.2.7 Synthesis of (±)-(2-Chlorophenyl)(2-dimethylphosphinophenyl)-methylphosphine [(±)-56]

Sodium foil (0.92 g, 0.04 mol) was added piecewise to a solution of (±)-(2-dimethylphosphinophenyl)methylphosphine, (±)-**66**, (7.38 g, 0.04 mol) in THF (100 mL) and the solution was stirred overnight. The resulting phosphide solution was filtered through a glass wool plug and added dropwise to a solution of 1,2-dichlorobenzene (5.89 g, 0.04 mol) in THF (40 mL). The reaction mixture was stirred for 5 days. Water (20 mL) was added, and the solvent removed under vacuum. Further water (90 mL) was added, and the aqueous phase was extracted with dichloromethane (3 x 90 mL). The organic extracts were dried ($MgSO_4$), filtered and the solvent removed to give a yellow oil. The crude oil was distilled under reduced pressure. Fraction 1 [b.p 40-80 °C (0.01 mmHg)]: a mixture of 1,2-dichlorobenzene, (±)-(2-methylphosphinophenyl)dimethylphosphine [(±)-**66**] and 1,2-phenylenebis(dimethylphosphine) (**68**). Yield 3.14 g. Fraction 2 [b.p 135 °C (0.001 mmHg)]: (±)-(2-chlorophenyl)(2-dimethylphosphinophenyl)methylphosphine [(±)-**56**]. Small quantities of **68** and **69** were also present. Yield 4.75 g (65% based on amount of **68** recovered). The distilled product was purified by complexation to nickel(II).

The ligand (±)-**56** (4.86 g, 16.2 mmol) was dissolved in deoxygenated ethanol (90 mL) and added dropwise to a solution of nickel(II) chloride hexahydrate (2.00 g, 8.41 mmol) in ethanol (20 mL). The red solution was stirred for 2 h. Excess ammonium hexafluorophosphate (2.06 g, 12.62 mmol) in water (10 mL) was added and the yellow/orange reaction mixture was stirred overnight. The product, which precipitated from solution, was filtered off and washed with water (15 mL), diethyl ether/methanol (10 mL) and diethyl ether (20 mL), and dried *in vacuo*. Further ammonium hexafluorophosphate (1.00 g, 6.13 mmol) in water (2 mL) was added to

the filtrate to afford an additional crop of crystals. The combined product was recrystallised from dichloromethane/diethyl ether to give pure [Ni{(±)-**56**}$_2$]. Yield 3.70 g (68%). M.p. 218 - 222 °C. Anal. calcd for $C_{28}H_{30}NiP_6F_{12}Cl_2$: C, 38.39; H, 3.65. Found C, 38.73; H, 3.84.

The complex [Ni{(±)-**56**}$_2$] (5.31 g, 5.97 mmol) was suspended in deoxygenated dichloromethane (50 mL) and water (60 mL). Potassium cyanide (17.63 g, 0.271 mol) was added and the solution was stirred vigorously for 15 h. The layers were separated and the aqueous layer extracted with dichloromethane (2 x 50 mL). The organic layers were combined, dried ($MgSO_4$), filtered and the solvent removed to give (±)-**56**. Yield 2.92 g (83%). ^{1}H NMR (d_6-benzene): δ 1.15 (d, 3 H, $^2J_{PH}$ 4.11 Hz, P*Me*), 1.22 (d, 3 H, $^2J_{PH}$ 3.36 Hz, P*Me*), 1.47 (d, 3 H, $^2J_{PH}$ 5.28 Hz, P*Me*C_6H_4Cl-2), 6.78 - 7.34 (m, 8 H, *aromatics*). ^{31}P {^{1}H} NMR (d_6-benzene): δ -53.6 (d, 1 P, $^3J_{PP}$ 153.6 Hz, *P*Me_2); -36.4 (d, 1 P, $^3J_{PP}$ 153.6 Hz, *P*MeC_6H_4Cl-2). m/e: 294 (M^+), 279 $(M-Me)^+$, 259 $(M-Cl)^+$.

5.2.8 Preparation of [SP-4-1]-Bis{(1,2-phenylenebis(dimethylphosphine)-P,P'}nickel(II) Hexafluorophosphate

The ligand **68** (0.544 g, 2.74 mmol) was dissolved in ethanol (10 mL) and hexaaquanickel(II) chloride (0.399 g, 1.37 mmol) was added. The solution was stirred for 2 h, filtered, and taken to dryness. The residue was redissolved in methanol and ammonium hexafluorophosphate (0.224 g, 1.37 mmol) in water (2 mL) was added dropwise. Water (15 mL) was added and the reaction mixture was stirred overnight. The product was filtered off, washed with water (10 mL), diethyl ether:methanol (4:1, 10 mL) and diethyl ether (15 mL), and dried *in vacuo*. Yield 0.542 g (66%). M.p. 314 - 317 °C. ^{1}H NMR (d_6-acetone): δ 2.19 (s, 24 H, P*Me*$_2$), 7.93 - 8.28 (d of m, 8 H, *aromatics*). ^{31}P{^{1}H} NMR (d_6-acetone): δ 41.2 (s, 4 P, *P*Me_2). Anal. calcd for $NiC_{20}H_{32}P_6F_{12}$: C, 32.23; H, 4.33. Found C, 32.14; H, 4.41.

5.2.9 Preparation of the resolving agent (-)-Di-μ-Chlorobis{(*S*)-[1-(dimethylamino)ethyl]phenyl-C^2N}dipalladium(II) [(*S*)-39]

The resolving agent (-)-di-μ-chlorobis{(*S*)-[1-(dimethylamino)ethyl]phenyl-C^2N}dipalladium(II) [(*S*)-**39**] was prepared by a literature procedure.[145]

Formic acid (98% w/v, 104 mL) was cooled to 0 °C and (*S*)-1-phenylethylamine (53 mL) was added with stirring. The solution was maintained at this temperature and after CO_2 evolution had ceased, formaldehyde (40% w/w, 129 mL) was added with stirring. The reaction mixture was allowed to warm to room temperature, then heated gently at 60 °C until CO_2 evolution ceased, and was then refluxed overnight. After cooling to 0 °C, hydrochloric acid (4 M, 250 mL) was added, and the solvent removed. Water (320 mL), then aqueous sodium hydroxide (91 g in 150 mL water) was added to the residual yellow oil, and the solution was extracted with dichloromethane (2 x 220 mL). The organic extracts were dried ($MgSO_4$), filtered, and the solvent was distilled off. The product, (*S*)-dimethyl[(1-(phenyl)ethyl]amine, was obtained as a colourless liquid, by distillation under reduced pressure. B.p. 50 ° C (0.3 mmHg). Yield 35.20 g, (57%). ^{1}H NMR (d_2-dichloromethane): δ 1.61 (d, 3 H, $^2J_{HH}$ 6.72 Hz, C*Me*), 2.45 (s, 6 H, N*Me*$_2$), 3.50 (d of d, 1 H, C*H*), 7.60 (m, 4 H, *aromatics*).

Palladium(II) chloride (25.00 g, 0.141 mol) and excess anhydrous lithium chloride (17.93 g, 0.423 mol) were suspended in methanol (350 mL) and stirred until dissolution was complete. The solution was filtered, and a mixture of (*S*)-dimethyl[1-(1-(phenyl)ethyl]amine (21.04 g, 0.141 mol) and triethylamine (14.26 g, 0.141 mol) was added dropwise. The mixture was left to stir overnight, and the product, which appeared as a yellow precipitate, was filtered off, washed with water (25 mL), diethyl ether/methanol (1:1, 20 mL), and diethyl ether (30 mL), and dried *in vacuo*. Yield 34.35 g (84%). ^{1}H NMR (d_6-dimethylsulfoxide): δ 1.21 (t, 3 H, $^2J_{HH}$ 7.20 Hz, C*Me*), 3.06 (m, 6 H, N*Me*$_2$), 3.94 (m, 1 H, C*H*), 6.99 - 7.62 (m, 4 H, *aromatics*).

5.2.10 Attempted Resolution of (±)-(2-Chlorophenyl)(2-dimethylphosphinophenyl)methylphosphine [(±)-56] using (*S*)-39. Formation of the Internally Diastereomeric Complexes [SP-4-3]-(S_P,*R*)-, [SP-4-3]-(R_P,*R*)-, [SP-4-4]-(S_P,*R*)- and [SP-4-4]-(R_P,*R*)-[(2-Chlorophenyl)(2-dimethylphosphinophenyl)methylphosphine-P,P']{[(1-dimethylamino)ethyl]phenyl-C^2,N}-palladium(II) Hexafluorophosphate

To a suspension of the resolving agent, di-μ-chlorobis{(*S*)-[1-(dimethylamino)ethyl]phenyl-C^2N}dipalladium(II) [(*S*)-**39**] (0.64 g, 1.09 mmol) in methanol (20 mL) was slowly added a solution of (±)-(2-chlorophenyl)(2-dimethylphosphinophenyl)methylphosphine [(±)-**56**] (0.64 g, 2.18 mmol) in methanol (50 mL). The mixture was stirred at room temperature for 2.5 h, and then filtered through celite. Excess ammonium hexafluorophosphate (0.50 g, 3.07 mmol) in water (5 mL) was added dropwise to the pale yellow filtrate. Water (50 mL) was added dropwise and the white precipitate that formed was left to stir overnight. The precipitate was filtered off, washed with water (15 mL), diethyl ether/methanol (5 mL) and diethyl ether (10 mL) and dried *in vacuo*. Yield 1.12 g (90%). $^{31}P\{^1H\}$ NMR (d_2-dichloromethane): δ 18.2 (d, $^2J_{PP}$ 25.6 Hz), 19.4 (d, $^2J_{PP}$ 24.7 Hz), 26.1 (d, $^2J_{PP}$ 24.7 Hz), 26.8 (d, $^2J_{PP}$ 25.6), 32.9 (d, $^2J_{PP}$ 24.7 Hz), 33.8 (d, $^2J_{PP}$ 22.8 Hz),

Separation of the four diastereomeric hexafluorophosphate salts [SP-4-3]-(R_P,*S*)-, [SP-4-3]-(S_P,*S*)-, [SP-4-4]-(R_P,*S*)- and [SP-4-4]-(S_P,*S*)-**70** could not be achieved by fractional crystallisation from a range of solvent systems.

5.2.11 Preparation of [SP-4-2]-(±)-Dichloro{(2-chlorophenyl)(2-dimethylphosphinophenyl)methylphosphine P,P'}palladium(II) [(±)-74]

The diastereomeric hexafluorophosphate salts [SP-4-3]-(R_P,*S*)-, [SP-4-3]-(S_P,*S*)-, [SP-4-4]-(R_P,*S*)- and [SP-4-4]-(S_P,*S*)-**70** (4.34 g, 7.90 mmol) were dissolved in acetone (20 mL) and hydrochloric acid (10 M, 2.5 mL) was added dropwise. The solution was heated on a steam bath for 10 mins, resulting in the precipitation of the product as a

yellow solid. When precipitation was completed, the product was filtered off, washed with water (10 mL), diethyl ether/methanol (4:1, 10 mL) and diethyl ether (15 mL), and dried *in vacuo*. Yield 3.392 g (91%). ^{1}H NMR (d_6-dimethylsulfoxide): δ 2.08 (6 H, $^{2}J_{PH}$ 13.92 Hz, PMe_2), 2.40 (d, 3 H, PMe), 7.51 - 8.23 (m, 8 H, aromatics). $^{31}P\{^{1}H\}$ NMR (d_6-dimethylsulfoxide) δ 53.5 (d, 1 P, $^{3}J_{PP}$ 17.0 Hz, *P*Me(2-ClC_6H_4)), 59.2 (d, 1 P, $^{3}J_{PP}$ 17.1 Hz, *P*Me_2).

5.2.12 Resolution of (±)-(2-Chlorophenyl)(2-dimethylphosphinophenyl)-methylphosphine [(±)-56] using (*S*)-72. Formation of the Internally Diastereomeric Complexes [SP-4-3]-(S_P,*R*)-, [SP-4-3]-(R_P,*R*)-, [SP-4-4]-(S_P,*R*)- and [SP-4-4]-(R_P,*R*)-[(2-Chlorophenyl)(2-dimethylphosphinophenyl)methyl-phosphine-P,P']{[(1-dimethylamino)ethyl]naphthyl-C^2,N}-palladium(II) Hexafluorophosphate

To a suspension of the resolving agent, di-μ-chlorobis{(*S*)-[1-(dimethylamino)ethyl]naphthyl-C^2N}dipalladium(II), [(*S*)-**72**] (2.51 g, 3.69 mmol) in methanol (30 mL), was slowly added a solution of (±)-(2-chlorophenyl)(2-dimethylphosphinophenyl)methylphosphine, [(±)-**56**] (2.18 g, 7.38 mmol) in methanol (90 mL). The mixture was stirred at room temperature for 2.5 h, and then filtered through celite. Excess ammonium hexafluorophosphate (1.51 g, 9.26 mmol) in water (10 mL) was added dropwise to the pale yellow filtrate. Water (70 mL) was added dropwise, and the white precipitate that formed was left to stir overnight. The precipitate was filtered off, washed with water (25 mL), diethyl ether/methanol (4:1, 15 mL) and diethyl ether (20 mL) and dried *in vacuo*. Yield 4.62 g (84%). $[\alpha]_D$ = +70° (c 1.0, dichloromethane).

The diastereomeric mixture of palladium(II) salts was dissolved in chloroform (30 mL) and propan-2-ol (20 mL) was added dropwise to give a 1:1 diastereomeric mixture of [SP-4-3]-(R_P,*S*)- and [SP-4-3]-(S_P,*S*)-**73** as fine white needles, which were filtered off, washed with diethyl ether (20 mL) and dried *in vacuo*. Yield 2.01 g (87%). $[\alpha]_D$ = +93° (c 1.0, dichloromethane). The mother liquor consisted of a *ca*

1:1:9:9 mixture of [SP-4-3]-(R_P,*S*)-, [SP-4-3]-(S_P,*S*)-, [SP-4-4]-(R_P,*S*)- and [SP-4-4]-(S_P,*S*)-**73** which could not be further separated by fractional crystallisation.

The 1:1 mixture of [SP-4-3]-(R_P,*S*)- and [SP-4-3]-(S_P,*S*)-**73** was dissolved in acetone (10 mL) and propan-2-ol (8 mL) was added dropwise until white blocks precipitated from solution. The mother liquor was decanted off and the blocks were dried under nitrogen to give diastereomerically pure [SP-4-3]-(S_P,*S*)-**73**. M.p. 217 - 220 °C. Yield 0.79 g (79%). $[\alpha]_D$ +74° (c 0.30, dichloromethane). ^{1}H NMR (d_6-acetone): δ 1.93 (d, 3 H, $^3J_{HH}$ 6.36 Hz, C*Me*), 2.11 (d, 3 H, $^2J_{PH}$ 8.43 Hz, PMe*Me*), 2.13 (d, 3 H, $^2J_{PH}$ 8.04 Hz, PMe*Me*), 2.36 (d, 3H, $^2J_{PH}$ 10.26, P*Me*), 2.97 (br s, 3 H, N*Me*), 3.42 (m, 3 H, N*Me*), 4.79 (m, 1 H, C*H*Me), 6.85 (d of d, 1 H, $^3J_{HH}$ 6.69 Hz, $^4J_{PH}$ 13.98 Hz, γ*H*), 7.28 - 8.44 (m, 13 H, *aromatics*). ^{31}P{^{1}H} NMR (d_6-acetone): δ 22.3 (d, 1 P, $^3J_{PP}$ 27.1 Hz, *P*Me$_2$), 38.0 (d, 1 P, $^3J_{PP}$ 20.6, *P*Me(C_6H_4Cl-2)). Anal calcd. for $PdC_{29}H_{33}P_3F_6NCl$: C, 46.79; H, 4.47, N, 1.88. Found C, 46.82; H, 4.37; N, 1.89.

The mother liquor, which was enriched in pure [SP-4-3]-(R_P,*S*)-**73**, was taken to dryness and the residue dissolved in dichloromethane (5 mL). Propan-2-ol (5 mL) was added dropwise until white plates precipitated from solution. The mother liquor was decanted off and the plates were dried under nitrogen to give diastereomerically pure [SP-4-3]-(R_P,*S*)-**73**. Yield 0.34 g (34%). M.p. 205 °C (decomp.). $[\alpha]_D$ +225° (c 0.30, dichloromethane). ^{1}H NMR (d_6-acetone): δ 1.87 (d, 3 H, $^3J_{HH}$ 6.30 Hz, C*Me*), 2.13 (d, 6 H, $^2J_{PH}$ 8.25 Hz, P*Me*$_2$), 2.57 (d, 3 H, $^2J_{PH}$ 9.57 Hz, P*Me*), 2.97 (br s, 3 H, N*Me*), 3.41 (t, 3 H, $^4J_{PH}$ 3.60 Hz, N*Me*), 4.78 (m, 1 H, C*H*Me), 7.33-8.50 (m, 14 H, *aromatics*). ^{31}P{^{1}H} NMR (d_6-acetone): δ 21.0 (d, 1P, $^3J_{PP}$ 27.1 Hz, *P*Me$_2$), 37.6 (d, 1P, $^3J_{PP}$ 21.7 Hz, *P*Me(C_6H_4Cl-2)). Anal. calcd for $PdC_{29}H_{33}P_3F_6NCl$ (+ CH_2Cl_2): C, 43.43; H, 4.25; N, 1.69. Found C, 43.78; H, 4.51; N, 1.70.

5.2.13 Preparation of [SP-4-2]-(S)-Dichloro{(2-chlorophenyl)(2-dimethylphosphinophenyl)methylphosphine P,P'}palladium(II) [(S_P)-74]

Diastereomerically pure [SP-4-3]-(R_P,*S*)-**73** (0.75 g, 1.01 mmol) was dissolved in concentrated sulfuric acid (4 mL) and the yellow solution was poured onto ice (10 g).

Lithium chloride (0.5 g, 11.78 mmol), dichloromethane (30 mL) and water (30 mL) was added, and the two layers were separated. The aqueous layer was further extracted with dichloromethane (2 x 30 mL), and the combined organic layers were combined, dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure. The residue was recrystallised from dichloromethane/methanol to give enantiomerically pure (S_P)-**74**. $[\alpha]_D$ = +52° (c 0.25, dichloromethane). Yield 0.40 g (85%). m.p. 180 - 185 °C. ^1H and $^{31}P\{^1H\}$ NMR (d_6-dimethylsulfoxide): identical with those recorded for the racemic compound (±)-**71**.

5.2.14 Isolation of (R)-(2-Chlorophenyl)(2-dimethylphosphinophenyl)-methylphosphine [(R_P)-56]

Enantiomerically pure (S_P)-**74** (0.40 g, 0.86 mmol) was suspended in petroleum spirit (60-80 °C) (20 mL) and methanol (20 mL). Potassium cyanide (2.24 g, 34.39 mmol) was added, and the mixture was shaken vigorously. Water (20 mL) was added and the layers were separated. The aqueous layer was extracted with petroleum spirit (2 x 30 mL). The organic layers were combined, dried, filtered and the solvent removed under vacuum to give (R_P)-**56**. $[\alpha]_D$ = +33° (c 0.25, dichloromethane). Yield 0.22 g (88%). ^1H and $^{31}P\{^1H\}$ NMR (d_6-benzene): identical with those recorded for the racemic compound (±)-**56**.

5.2.15 Synthesis of (±)-(R_P*,R_P*)-1,2-Bis[(2-dimethylphosphinophenyl)-methylphosphino]benzene [(R_P*,R_P*)-57]

Excess sodium foil (0.302 g, 13.13 mmol) was added to a solution of (±)-(2-dimethylphosphinophenyl)methylphosphine, (±)-**66**, (2.29 g, 12.42 mmol) in THF (50 mL). The solution was stirred overnight and then added, via a dropping funnel containing a glass wool plug, to a solution of (±)-(2-chlorophenyl)(2-dimethylphosphinophenyl)methylphosphine, (±)-**56**, (3.48 g, 11.81 mmol) in THF (50

mL) at -78 °C. The dark red solution was allowed to warm to room temperature and stirred for 7 days, by which time the reaction mixture was a very pale yellow. The solvent was distilled off under argon, and water (100 mL) was added. The residue was extracted with dichloromethane (2 x 100 mL) and diethyl ether (100 mL). The organic extracts were combined, dried ($MgSO_4$), filtered, and the solvent distilled off under argon to leave a colourless oil and white solid. m/e: 442 $(M)^+$, 427 $(M\text{-}Me)^+$, 381 $(M\text{-}PMe_2)^+$, 305 $(M\text{-}C_6H_4PMe_2)^+$.

The crude product was dissolved in hot methanol (150 mL), and a solution of hexaaquacobalt(II) chloride [3.09 g, 12.99 mmol (10% excess)] was added dropwise and the reaction mixture stirred for 1 h. Hydrochloric acid (10M, 6 mL) was added and air was drawn through the solution for 4.5 h. The solvent was removed under reduced pressure. Water (120 mL) was added to the residue, and the mixture was refluxed for 4 h. The solution was allowed to cool to room temperature overnight. The silver-grey precipitate, *trans*-$[CoCl_2(\mathbf{68})_2]Cl$, was filtered off and washed with cold water. The filtrate was left at 5 °C for 2 days, resulting in the further precipitation of *trans*-$[CoCl_2(\mathbf{68})_2]Cl$, which was filtered off. The isolated complexes were combined and recrystallised from methanol (200 mL), filtered, washed with diethyl ether (20 mL) and dried *in vacuo*. Yield 1.65 g (49%). m.p. 312 - 317 °C. ^1H NMR (d_4-methanol): δ 1.98 (s, 12 H, P*Me*), 7.85 - 8.24 (d of m, 8 H, *aromatics*). $^{31}P\{^1H\}$ NMR (d_4-methanol): δ 54.9 (s, 4 P, PMe_2).

The red filtrate was left standing for 2 weeks, resulting in precipitation of red rosettes of *cis*-α-(±)-$[CoCl_2\{(R_P^*,R_P^*)\text{-}\mathbf{57}\}]Cl$, which were filtered off and washed with diethyl ether. Yield 0.67 g (16%). m.p. 310 - 312 °C. ^1H NMR (d_4-methanol): δ 1.90 (d of d, $^2J_{PH}$ 4.17 Hz, 6 H, 2 P*Me*), 2.23 (t, 6 H, $|^2J_{PH} + {}^4J_{P'H}|$ 10.9 Hz, 2 PMe*Me*), 2.27 (t, 6 H, $|^2J_{PH} + {}^4J_{P'H}|$ 15.6 Hz, 2 P*Me*Me), 7.76 - 8.53 (m, 12 H, aromatics). $^{31}P\{^1H\}$ NMR (d_4-methanol): δ 58.6 (bs, 2 P, 2 PMe_2), 96.5 (bs, 2 P, 2 *P*Me).

5.2.16 Preparation of [OC-6-22-(R_P*,R_P*)]-(±)-Dichloro{1,2-bis[(2-dimethylphosphinophenyl)methylphosphino]benzene-P,P',P'',P'''}cobalt(III) Hexafluorophosphate

The chloride salt *cis*-α-[$CoCl_2${(R_P*,R_P*)-**57**}]Cl (0.20 g, 0.33 mmol) was dissolved in methanol (20 mL) and ammonium hexaflourophosphate (0.11 g, 0.66 mmol) in water (1 mL) was added dropwise. Water (20 mL) was added and the solution was stirred for 30 mins. The product was filtered off, washed with water (5 mL), diethyl ether/methanol (4:1, 5 mL) and diethyl ether (10 mL), and dried *in vacuo*. Yield 0.21 g (88%). M.p. 310 - 312 °C. ^{1}H NMR (d_6-acetone): δ 2.09 (d of d, $^2J_{PH}$ 4.17 Hz, 6 H, 2 P*Me*), 2.31 (t, 6 H, $|^2J_{PH} + {}^4J_{P'H}|$ 15.6 Hz, 2 P*Me*Me), 2.43 (t, 6 H, $|^2J_{PH} + {}^4J_{P'H}|$ 15.6 Hz, 2 PMe*Me*), 7.76 - 8.53 (m, 12 H, *aromatics*). ^{31}P{^{1}H} NMR (d_2-dichloromethane): δ 58.7 (bs, 2 P, 2 *P*Me_2), 92.8 (bs, 2 P, 2 *P*Me). Anal. calcd for $C_{24}H_{30}F_6Cl_2CoP_5$: C, 40.19; H, 4.22. Found: C, 39.90; H, 4.15.

5.2.17 Preparation of (2-Chlorophenyl)diphenylphosphine (76)

The tertiary phosphine (2-chlorophenyl)diphenylphosphine (**76**) was prepared by a modified literature procedure.[123]

To a suspension of magnesium turnings (6.35 g, 0.26 mol) in diethyl ether (50 mL) was added 1-bromo-2-chlorobenzene (50.00 g, 0.26 mol) dropwise. Further diethyl ether (300 mL) was added during the course of the addition to prevent precipitation of the resulting Grignard reagent. The solution was refluxed for 20 mins, then cooled to 0 °C. A solution of chlorodiphenylphosphine (57.62 g, 0.26 mol) was added dropwise, and the solution was heated for 20 mins. Saturated aqueous ammonium chloride solution (30 mL), then water (60 mL) was added, and the layers were separated. The aqueous layer was extracted with diethyl ether (3 x 70 mL). The organic layers were combined, dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure. The solid residue was recrystallised from hot ethanol (170 mL) and left at 5 °C overnight to give the product as an off-white powder. The

product was filtered off, washed with cold ethanol (30 mL), and dried *in vacuo*. The filtrate was reduced in volume and left at 5 °C overnight to give a further crop of product. Yield 50.42 g (65%). M.p. 103 - 105 °C (lit.[123] 106 - 108 °C). ^{1}H NMR (d_1-chloroform): δ 6.73 - 7.42 (m, 14 H, *aromatics*). ^{31}P{^{1}H} NMR (d_1-chloroform): δ -10.3 (s, 1 P).

5.2.18 Synthesis of (±)-(R_P*,R_P*)-1,2-Bis[(2-diphenylphosphinophenyl)-methylphosphino]benzene [(R_P*,R_P*)-58]

Excess sodium foil (1.48 g, 0.064 mol) was added to (R_P*,R_P*)- and (R_P*,S_P*)- 1,2-phenylenebis(methylphosphine), (R_P*,R_P*)- and (R_P*,S_P*)-**65**, (4.66 g, 0.027 mol) in THF (120 mL). The solution was stirred for 48 h, then cooled to -78 °C, and (2-chlorophenyl)diphenylphosphine, **76**, (18.26 g, 0.062 mol) in THF (250 mL) was added over a period of 1.5 h. The dark red solution was allowed to slowly come to room temperature and stirred for 15 days, by which time the solution had turned orange. The reaction mixture was then cooled to 0 °C, and saturated aqueous ammonium chloride solution (20 mL) was added. The solvent was distilled off under argon, and water (200 mL) was added to the residue. The residue was extracted with dichloromethane (2 x 100 mL) and diethyl ether (100 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and the solvents were distilled off under argon. The residue, consisting of an orange oil and a white solid material, was refluxed in methanol (400 mL) for 4 h. The solution was allowed to cool overnight to give the product as a white micro-crystalline material. The product was filtered off under argon, washed with methanol (50 mL) and dried *in vacuo* at 40 °C for 24 h. Yield 6.18 g (33%). M.p. 114 - 116 °C. ^{1}H NMR (d_6-benzene): δ 1.74 (m, 6 H, P*Me*), 6.90 - 7.46 (m, 32 H, *aromatics*). ^{31}P{^{1}H} NMR (d_6-benzene): δ_A -36.1 (internal P; AA'), δ_X -14.1 (terminal P; XX'), (AXX'A'), $J_{AA'}$ 140.0 Hz, J_{AX} 149.5 Hz, $J_{A'X}$ 6.9 Hz, $J_{XX'}$ 0.0 Hz). Anal calcd. for $C_{44}H_{38}P_4$: C, 76.52; H, 5.55. Found C, 76.36, H, 5.85. m/e: 690 $(M)^+$, 675 $(M\text{-}Me)^+$, 613 $(M\text{-}Ph)^+$, 505 $(M\text{-}PPh_2)^+$, 383 $(M\text{-}PPh_2)^+$.

5.2.19 Preparation of [OC-6-22-(R_P*,R_P*)]-(±)-Dichloro{1,2-bis[(2-diphenylphosphinophenyl)methylphosphino]benzene-P,P',P'',P'''}cobalt(III) Chloride Trihydrate and [OC-6-22-(R_P*,R_P*)]-(±)-Dichloro{1,2-bis{[1-(2-diphenylphosphinoylphenyl)-2-(2-diphenylphosphinophenyl)]methyl-phosphino}benzene- O,P,P',P''}cobalt(III) Chloride Tetrahydrate

The ligand (R_P*,R_P*)-**58** (0.75 g, 1.09 mmol) was suspended in methanol (30 mL), and a solution of hexaaquacobalt(II) chloride (0.26 g, 1.09 mmol) in methanol (5 mL) was added dropwise. Hydrochloric acid (10 M, 4 mL) was added, and the solution was stirred for 1.5 h. Air was then drawn through the solution for 4 h. The solvent was removed under vacuum, and water (40 mL) was added to the residue. The mixture was refluxed for 4 h and then allowed to cool to room temperature overnight. The resulting red-brown powder, which was a *ca* 2:1 mixture of *cis*-α-[$CoCl_2${(R_P*,R_P*)-**58**}]Cl.3H_2O and *cis*-α-[$CoCl_2${(R_P*,R_P*)-**58***}]Cl.4H_2O, was filtered off, washed with water (5 mL), diethyl ether/methanol (4:1, 5 mL) and diethyl ether (5 mL), and dried *in vacuo*. Yield 0.641 g (69%).

The mixture of complexes was dissolved in hot methanol (60 mL) and the red solution was boiled down to 20 mL. The solution was left to stand for 72 h, resulting in the precipitation of fine red crystals of *cis*-α-[$CoCl_2${(R_P*,R_P*)-**58**}]Cl.3H_2O, which were filtered off, washed with water (3 mL), diethyl ether/methanol (4:1, 2 mL) and diethyl ether (10 mL), and dried *in vacuo*. Yield 0.385 g (42%). M.p. 319 - 322 °C. ^{1}H NMR (d_6-dimethylsulfoxide): δ 0.96 (6 H, $^2J_{PH}$ 6.6 Hz, 2 P*Me*), 7.00 - 8.57 (m, 32 H, *aromatics*). $^{31}P\{^1H\}$ NMR (d_6-dimethylsulfoxide): δ 60.5 (bs, 2 P, 2 *P*Ph_2), 90.0 (bs, 2 P, 2 *P*Me). Anal. calcd for $C_{44}H_{45}Cl_3CoO_{3.5}P_4$: C, 57.48; H, 4.94. Found C, 57.37, H, 4.48.

The filtrate from the isolation of *cis*-α-[$CoCl_2${(R_P*,R_P*)-**58**}]Cl.3H_2O was reduced in volume by *ca* 50% and allowed to stand for 72 h, whereupon dark red crystals of *cis*-α-[$CoCl_2${(R_P*,R_P*)-**58***}]Cl.4H_2O precipitated from solution. The crystals were filtered off and washed with water (5 mL), diethyl ether/methanol (4:1, 5 mL) and diethyl ether (5 mL). Yield 0.172 g (18%). M.p. 313 - 315 °C (decomp.). ^{1}H NMR (d_6-dimethylsulfoxide): δ 0.85 (d, 3 H, $^2J_{PH}$ 13.64 Hz, P*Me*); 2.35 (d, 3 H, $^2J_{PH}$ 14.28

Hz, P*Me*); 7.75 - 9.00 (m, 32 H, *aromatics*). $^{31}P\{^{1}H\}$ NMR (d_6-dimethylsulfoxide): δ 43.0 (s, 1P, *P*(O)Ph_2); 46.8 (m, 1 P, *P*Me); 52.9 (t, 1P, *P*Ph_2); 97.2 (t, 1 P, $^{3}J_{PP}$ 56.3 Hz, *P*Me). Anal. calcd for $C_{44}H_{46}Cl_3CoO_5P_4$: 55.96; H, 4.91. Found C, 55.63; H 4.66.

5.2.20 Preparation of [OC-6-22-(R_P*,R_P*)]-(±)-Dichloro{1,2-bis[(2-diphenylphosphinophenyl)methylphosphino]benzene-P,P',P'',P'''}cobalt(III) Hexafluorophosphate

The chloride salt *cis*-α-[$CoCl_2${(R_P*,R_P*)-**58**}]Cl.3H_2O (0.322 g, 0.380 mmol) was suspended in methanol (25 mL) and a solution of ammonium hexafluorophosphate (0.124 g, 0.760 mmol) in water (1 mL) was added dropwise. Water (20 mL) was added and the solution was stirred overnight. The product was filtered off, washed with water (5 mL), diethyl ether/methanol (4:1, 5 mL) and diethyl ether (5 mL), and dried *in vacuo*. Yield 0.316 g (86%). M.p 317 - 320 °C. ^{1}H NMR (d_2-dichloromethane): δ 0.94 (m, 6 H, 2 P*Me*), 7.14 - 8.23 (m, 32 H, *aromatics*). $^{31}P\{^{1}H\}$ NMR (d_2-dichloromethane): δ 58.5 (bs, 2 P, 2 *P*Ph_2), 87.9 (bs, 2 P, 2 *P*Me). Anal. calcd for $C_{44}H_{38}F_6Cl_2CoP_5$: C, 54.74; H, 3.97%. Found: C, 54.69; H, 4.09.

5.2.21 Synthesis of (±)-(2-Chlorophenyl)methylphenylphosphine [(±)-77]

The tertiary phosphine (±)-(2-chlorophenyl)methylphenylphosphine [(±)-**77**] was prepared by a modified literature procedure.[120]

A slight excess of sodium foil (6.03 g, 0.262 mol) was added to (±)-methylphenylphosphine (32.18 g, 0.259 mol) in THF (500 mL) and the solution was stirred overnight. The resulting phosphide solution was filtered through a glass wool plug and added dropwise to a solution of 1,2-dichlorobenzene (51.32 g, 0.349 mol) in THF (50 mL), at -78 °C. The solution was allowed to warm to room temperature, and

was stirred overnight to give a red/brown solution. The solvent was distilled off under argon, and water (200 mL) was added to the residue. The aqueous layer was extracted with dichloromethane (3 x 100 mL). The dichloromethane extracts were dried ($MgSO_4$), filtered and the solvent distilled off under argon to leave a red oil. The crude oil was distilled under vacuum. Fraction 1 [b.p 40-42 °C (0.02 mmHg)]: a mixture of 1,2-dichlorobenzene and (±)-methylphenylphosphine. Fraction 2 [b.p 112 °C (0.02 mmHg) (lit.[120] 126 - 128 °C (0.05 mmHg))]: (±)-(2-chlorophenyl)methylphenylphosphine [(±)-**77**]. Yield 37.89 g (62%). ^{1}H NMR (d_1-chloroform): δ 1.62 (d, 3 H, $^2J_{PH}$ 4.53 Hz, P*Me*), 7.1 - 7.5 (m, 9 H, *aromatics*). $^{31}P\{^1H\}$ NMR (d_1-chloroform): δ -31.0 (s, 1 P). M/e 234 $(M)^+$, 219 $(M\text{-}Me)^+$, 199 $(M\text{-}Cl)^+$.

5.2.22 Synthesis of (R_P*,R_P*,R_P*,S_P*)- and (R_P*,S_P*,S_P*,R_P*)-1,2-Bis[(2-methylphenylphosphino)methylphosphino]benzene [(R_P*,R_P*,R_P*,S_P*)- and (R_P*,S_P*,S_P*,R_P*)-**59**]

Sodium foil (1.50 g, 0.065 mol) was added to a solution of (R_P*,R_P*)- and (R_P*,S_P*)-1,2-phenylenebis(methylphosphine), (R_P*,R_P*)- and (R_P*,S_P*)-**65**, (5.56 g, 0.033 mol) in THF (200 mL). The mixture was stirred for 48 h. Any excess sodium pieces were removed and the solution was cooled to -78 °C. A solution of (±)-(2-chlorophenyl)methylphenylphosphine, (±)-**77**, (13.02 g, 0.065 mol) in THF (100 ml) was added dropwise over a period of 1.5 h. The reaction mixture was allowed to slowly warm to room temperature and stirred for 14 days, to give a light orange solution.

The solution was cooled to 0 °C, and saturated aqueous ammonium chloride solution (25 mL) was added. The solution went colourless and the solvent was distilled off under argon. Water (200 mL) was added to the residue, which was extracted with dichloromethane (2 x 100 mL) and diethyl ether (100 mL). The combined organic extracts were dried ($MgSO_4$), filtered and the solvents distilled off under argon, to

leave a yellow oil and white solid as residue. M/e 566 $(M)^+$, 551 $(M\text{-}Me)^+$, 443 $(M\text{-}PMePh)^+$, 367 $(M\text{-}C_6H_4PMePh)^+$, 321 $(M\text{-}P(Me)(C_6H_4PMePh))^+$.

The residue was taken up in methanol (170 mL) and a solution of hexaaquacobalt(II) chloride (8.66 g, 0.036 mol) in methanol (40 mL) was added with stirring. Hydrochloric acid (10 M, 30 mL) was added dropwise, and the mixture was stirred for 30 mins. Air was drawn through the solution for 4 h, and the solvents were then removed under reduced pressure. The residual gum was taken up in methanol (300 mL). A quarter of the solution (75 mL) was loaded onto an ion-exchange column containing a Dowex-50WX8 200 mesh resin, and eluted with 0.2 M HCl/methanol. The cis-α complexes *cis*-α-$[CoCl_2\{(R_P*,R_P*,R_P*,S_P*)$-**59**$\}]Cl$ and *cis*-α-$[CoCl_2\{(R_P*,S_P*,S_P*,R_P*)$-**59**$\}]Cl$ were obtained as a red band. Yield 1.465 g (24%)

The cis-α complexes were dissolved in methanol, loaded onto an ion exchange column (Dowex-50WX8, 200 mesh resin) and eluted with 0.075 M HCl/methanol. The first and major band eluted was *cis*-α-$[CoCl_2\{(R_P*,R_P*,R_P*,S_P*)$-**59**$\}]Cl$. Yield 1.00 g (17%). ^1H NMR (d_4-methanol): δ 0.92 (d, 3 H, $^2J_{PH}$ 13.17 Hz, P*Me*), 2.40 (d, 6 H, $^2J_{PH}$ 10.20 Hz, P*Me*Ph), 2.48 (d, 3 H, $^2J_{PH}$ 10.32 Hz, P*Me*), 7.15 - 8.55 (m, 22 H, *aromatics*). $^{31}P\{^1H\}$ NMR (d_4-methanol): δ 61.9 (br m, 2 P, *P*ArPhMe), 90.5 (m, 1 P, *P*Me), 97.1 (m, 1 P, *P*Me).

The second, minor band eluted was *cis*-α-$[CoCl_2\{(R_P*,S_P*,S_P*,R_P*)$-**59**$\}]Cl$. Yield 0.09 g (2%). M.p. 220 - 225 °C. ^1H NMR (d_4-methanol): δ 2.18 (t, 6 H, $^2J_{PH}$ 3.84 Hz, P*Me*), 2.45 (t, 6 H, $^2J_{PH}$ 6.6 Hz, P*Me*), 7.20 - 8.46 (m, 22 H, *aromatics*). $^{31}P\{^1H\}$ NMR (d_4-methanol): δ 59.6 (br s, 2 P, *P*MePh), 92.5 (br s, 2 P, *P*Me).

5.2.23 Preparation of [OC-6-22-(R_P*,R_P*,R_P*,S_P*)]-(±)-Dichloro{1,2-bis[(2-methylphenylphosphinophenyl)methylphosphino]benzene-P,P',P'',P'''}-cobalt(III) Hexafluorophosphate

A solution of ammonium hexafluorophosphate (0.07 g, 0.41 mmol) in water (1 mL) was added to a solution of *cis*-α-[$CoCl_2$\{(R_P*,R_P*,R_P*,S_P*)-**59**\}]Cl (0.25 g, 0.34 mmol) in methanol (15 mL). Water (25 mL) was added and the solution was stirred for 2 h. The product was filtered off, washed with water (5 mL), diethyl ether:methanol (4:1, 5 mL) and diethyl ether (10 mL), and dried *in vacuo*. Yield 0.20 g (66%). M.p. 248 - 252 °C. ^{1}H NMR (d_2-dichloromethane): δ 0.85 (d, 3 H, $^2J_{PH}$ 12.63, P*Me*), 2.29 (d, 6 H, $^2J_{PH}$ 10.56 Hz, P*Me*Ph), 2.49 (d, 3 H, $^2J_{PH}$ 8.37 Hz, P*Me*), 7.00-8.30 (m, 22 H, *aromatics*). ^{31}P{^{1}H} NMR (d_2-dichloromethane): δ 60.8 (br s, 2P, *P*PhMe), 88.1 (br s, 1 P, *P*Me), 95.3 (br s, 1 P, *P*Me). Anal. calcd. for $CoC_{34}H_{34}P_5Cl_2F_6$ [+0.5 $(CH_3CH_2)O$]: C, 49.26, H, 4.37. Found: C, 49.32, H, 4.15.

5.2.24 Preparation of [OC-6-22-(R_P*,R_P*)]-(±)-Dichloro{1,2-bis[(2-diphenylphosphinophenyl)methylphosphino]benzene-P,P',P'',P'''}-ruthenium(II)

The ligand (R_P*,R_P*)-**58** (0.81 g, 1.18 mmol) was added to a refluxing solution of *cis*-[$RuCl_2(DMSO)_4$] (0.57 g, 1.18 mmol) in methanol (100 mL), and the reaction mixture was heated under reflux for 2 h. The reaction mixture was then allowed to cool to room temperature, and the resulting precipitate, which was a mixture of *cis*-α-$RuCl_2$\{(R_P*,R_P*)-**58**\} and *cis*-α-[RuCl(DMSO)\{(R_P*,R_P*)-**58**\}]Cl, was filtered off, washed with diethyl ether (10 mL) and dried *in vacuo*.

The crude product was dissolved in boiling methanol (170 mL), and hydrochloric acid (10M, 4 mL) was added dropwise. The solution was heated under reflux for 2 h, then allowed to cool to room temperature. The product was filtered off, washed with water (10 mL), diethyl ether:methanol (4:1, 5 mL), and diethyl ether (5 mL), and dried *in vacuo*. Yield 0.67 g (66%). M.p. >350 °C. ^{1}H NMR (d_2-dichloromethane): δ 0.97

(t, 6 H, $^{2}J_{PH}$ 5.07 Hz, P*Me*), 7.05 - 8.31 (m, 32 H, *aromatics*). $^{31}P\{^{1}H\}$ NMR (d_2-dichloromethane): δ 53.2 (t, 2 P, $^{3}J_{PP}$ 19.1 Hz, *P*Ph_2), 84.1 (t, 2 P,$^{3}J_{PP}$ 20.6 Hz, *P*Me). Anal. calcd for $RuC_{44}H_{38}P_4Cl_2$ [+2 $(CH_3CH_2)_2O$]: C, 61.76; H, 5.79. Found: C, 62.22; H, 5.79.

5.2.25 Preparation of [T-4-(R_P*,R_P*)]-(±)-{1,2-Bis[(2-diphenylphosphino-phenyl)methylphosphino]benzene-P,P',P'',P'''}gold(I) Hexafluorophosphate

The ligand (R_P*,R_P*)-**58** (0.15 g, 0.22 mmol) was added to a solution of tetrabutylammonium diiodoaurate (0.15 g, 0.22 mmol) in ethanol (10 mL) and the solution was stirred for 2 h. A solution of ammonium hexafluorophosphate (0.06 g, 0.36 mmol) in water (1 mL) was added and the solution was stirred overnight. The product, which precipitated as a white solid, was filtered off and dried *in vacuo*. Yield 0.18 g (81%). M.p. 288 °C. ^{1}H NMR (d_6-acetone): δ 1.97 (bs, 6 H, P*Me*), 7.59 - 8.55 (m, 32 H, *aromatics*). $^{31}P\{^{1}H\}$ NMR (d_6-acetone): δ_A 23.6 (internal P; AA'), δ_X 3.7 (terminal P; XX'), (AXX'A'), $J_{AA'}$ 41 Hz, J_{AX} 131 Hz, $J_{A'X}$ 75 Hz, $J_{XX'}$ 7 Hz. Anal. calc for $C_{44}H_{38}AuF_6P_5.H_2O$: C, 49.45: H, 3.96. Found: C, 49.14: H, 3.60. m/e 888 $(M)^{+}$.

5.2.26 Preparation of [T-4-(R_P*,R_P*)]-(±)-{1,2-Bis[(2-diphenylphosphino-phenyl)methylphosphinoyl]benzene-O,O',P,P'}silver(I) Hexafluorophosphate and [T-4-(R_P*,R_P*)]-(±)-{1,2-Bis[(2-diphenylphosphinophenyl)methyl-phosphino]benzene-P,P',P'',P'''}silver(I) Hexafluorophosphate

Silver nitrate (0.04 g, 0.22 mmol) was dissolved in ethanol (50 mL) and (R_P*,R_P*)-**58** (0.15 g, 0.22 mmol) was added with stirring. When the solid had dissolved, the solvent was removed and the residue redissolved in dichloromethane (7 mL). Ammonium hexafluorophosphate (0.04 g, 0.25 mmol) in water (2 mL) was added and the solution was stirred for 2 h. Further dichloromethane (10 mL) and water (10 mL) was added, the layers were separated and the organic layer was taken to dryness. The

resultant white precipitate, which was a mixture of [Ag{(R_P*,R_P*)-**58**}]PF_6 and [Ag{(R_P*,R_P*)-**58***}]PF_6, was collected, washed with water (3 mL), diethyl ether:methanol (4:1, 5 mL) and diethyl ether (5 mL), and dried *in vacuo*. Yield 0.16 g (77%). M.p. 175 °C. ^{1}H NMR (d_6-acetone): δ 1.51 (s, 6 H, P*Me*), 7.36 - 8.60 (m, 32 H, *aromatics*). ^{31}P{^{1}H} NMR (d_6-acetone): δ 45.5 (s, 2 P, *P*O(Me_2)), 13.1 [d of d, ^{1}J(^{107}Ag-^{31}P) -377 Hz, ^{1}J(^{109}Ag-^{31}P) -433 Hz, 2 P, *P*Ph_2], 5.1 [^{1}J(^{107}Ag-^{31}P) -517 Hz, ^{1}J(^{109}Ag-^{31}P) -597 Hz, $^3J_{PP}$ 147 Hz, $^1J_{PP}$ 75 Hz, *P*Ph_2], -32.7 - -33.3 ($^3J_{AB}$ 89 Hz, *P*Me).

5.2.27 Attempted Resolution of (R_P*,R_P*)-(±)-1,2-Bis[(2-diphenylphosphinophenyl)methylphosphino]benzene with (*S*)-39. Formation of the Internally Diastereomeric Complexes {[(2-diphenylphosphinophenyl)-methylphosphino]benzene-P,P',P'',P'''}bis{[(*S*)-(1-dimethylamino)ethyl]phenyl-C^2,N}dipalladium(II) Hexafluorophosphate

The tetra(tertiary phosphine) (R_P*,R_P*)-**58** (0.99 g, 1.44 mmol) was suspended in methanol (25 mL) and a suspension of the resolving agent (+)-di-μ-chlorobis{(*S*)-[1-(dimethylamino)ethyl]phenyl-C^2N}dipalladium(II), (*S*)-**39**, (0.83 g, 1.44 mmol) in methanol (10 mL) was added. The reaction mixture was stirred overnight, then filtered through celite. A solution of ammonium hexafluorophosphate (0.25 g, 1.53 mmol) in water (2 mL) was added to the yellow filtrate. Water (30 mL) was added and the solution was stirred for 2 h. The resulting precipitate was filtered off, washed with water (15 mL), diethyl ether:methanol (4:1, 10 mL) and diethyl ether (15 mL), and dried *in vacuo*. Yield 1.63 g (76%). M.p. 205 - 210 °C. ^{1}H NMR (d_2-dichloromethane): δ 1.16 (d, $^2J_{HH}$ 6.09, C*Me*), 1.26 (d, $^2J_{HH}$ 6.18 Hz, C*Me*), 1.33 (d, $^2J_{HH}$ 5.91, C*Me*), 1.46 (d, $^2J_{HH}$ 6.03, C*Me*), 1.52 (br s, P*Me*), 1.69 (d, $^2J_{PH}$ 5.73, P*Me*), 1.88 (br s, P*Me*), 2.03 (br s, P*Me*), 2.27-2.92 (m, 6 H, N*Me*), 3.37 (m, C*H*), 3.60 (m, C*H*), 3.89 (m, C*H*), 4.50 (m, C*H*), 5.82 - 8.58 (m, 40 H, *aromatics*). Anal. calcd for $Pd_2C_{64}H_{66}P_6F_{12}N_2$: C, 51.57; H, 4.46; N, 1.88. Found C, 51.69; H, 4.37; N, 2.11. M/e 1345.2 $(M\text{-}PF_6)^+$.

Separation of the internally diastereomeric palladium(II) salts could not be achieved by fractional crystallisation, from a range of solvent systems.

5.2.28 Preparation of (1,5-Cyclooctadiene)dimethylplatinum(II)

The complex (1,5-cyclooctadiene)dimethylplatinum(II) was prepared by a modified literature procedure.[146]

To a suspension of (1,5-cyclooctadiene)diiodoplatinum(II) (0.88 g, 1.58 mmol) in dry benzene (15 mL), was added a solution of excess Grignard reagent [prepared from magnesium (0.22 g, 9.00 mmol) and methyl iodide (1.28 g, 9.00 mmol) in diethyl ether (25 mL)], *via* a canula. The murky yellow solution was stirred for 1 h. The reaction was quenched by the dropwise addition of methanol (30 mL), and the solvent was then removed under reduced pressure. The residual solid was extracted with hot petroleum spirit (4 x 50 mL), the solution filtered and then reduced in volume by evaporation on a steam bath, until crystallisation occurred. Crystallisation was completed at -5 °C overnight. The resulting white needles were filtered off and dried *in vacuo*. Yield 0.37 g (70%). M.p. 90 - 92 °C (lit.[146] 94 - 95 °C). ^{1}H NMR (d_1-chloroform): δ 0.72 (s, 6 H, $^2J_{PtH}$ 69 Hz, Pt*Me*); 2.30 (m, 8 H, CH_2); 4.80 (s, 4 H, *H*C=C*H*)

4.2.29 Preparation of [SP-4-2-(R_P*,R_P*)]-(±)-{1,2-Bis[(2-diphenylphosphinophenyl)methylphosphino]benzene-P,P'}dimethylplatinum(II)

The ligand (R_P*,R_P*)-**58** (0.10 g, 0.15 mmol) was added to a solution of (1,5-cyclooctadiene)dimethylplatinum(II) (0.05 g, 0.15 mmol) in petroleum spirit (b.p 40 - 60 °C, 7 mL). The reaction mixture was stirred overnight, and the resulting product was filtered off, washed with petroleum spirit (b.p 40 - 60 °C, 5 mL), and dried *in vacuo*. Yield 0.12 g (86%). M.p. 145 - 150 °C (decomp.). ^{1}H NMR (d_2-dichloromethane): δ 0.15 (s, 6 H, $^2J_{PtH}$ 62.5 Hz, Pt*Me*); 2.10 (br d, 6 H, $^2J_{PH}$ 4.92 Hz,

$^{3}J_{PtH}$ 46.7, P*Me*); 6.75 - 8.50 (m, 32 H, *aromatics*). $^{31}P\{^{1}H\}$ NMR (d_2-dichloromethane): δ -13.0 (d, 2 P, $^{3}J_{PP}$ 75 Hz, 2 *P*Ph_2), 30.0 (d, 2 P, $^{1}J_{PtP}$ 1693 Hz, $^{3}J_{PP}$ 75 Hz, 2 *P*Me). Anal. calcd for $C_{46}H_{44}P_4Pt$: C, 60.19; H, 4.84. Found C, 60.33, H, 4.85.

Chapter Six

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6.1 REFERENCES

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